ANNALS OF INTERNAL MEDICINE

PUBLISHED MONTHLY BY

The American College of Physicians

Publication Office: Prince and Lemon Sts., Lancaster, Pa.
Executive Office: 4200 Pine Street, Philadelphia, Pa.

VOL. 13 (O.S., Vol. XVIII) APRIL, 1940 NUMBER 10

CONTENTS

Subscription per volume or per annum, net postpaid, $7.00, United States, Canada, Mexico, Cuba, Canal Zone, Hawaii, Puerto Rico; $7.50, other countries.

Entered as Second Class Matter at the Post Office at Lancaster, Pa. Acceptance for mailing at a special rate of postage provided for in the Act of February 28, 1925, embodied in paragraph 4, section 538, P. L. & R., authorized October 7, 1936.

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(Continued on Inside Back Cover)

ANNALS OF
INTERNAL MEDICINE

VOLUME 13 APRIL, 1940 NUMBER 10

WHAT IS AN INTERNIST? *

By O. H. PERRY PEPPER, M.D., F.A.C.P., *Philadelphia, Pennsylvania*

PRESIDENTS annually come and, fortunately for you, Presidents annually go. Each performs his duties as well as he can; each meets certain problems which he solves if he can, and each year at the Convocation the President addresses you on the state of the College or on some phase of our College or professional activity. As one reads the Presidential Addresses of past years, one is impressed by the learning and wisdom of my predecessors in this office. They have settled all sorts of tremendous problems—political, ethical, medical, sociological—the discussion of which required the utmost bravery. On the other hand, these brilliant gentlemen have demonstrated a marked degree of timidity in one direction. As one reads their addresses, one sees them getting closer and closer to a certain question, then suddenly turning away and avoiding it. This is quite amazing for this question is of some importance to our College and to each of us, for it concerns what we are and what we do.

Like these former Presidents, I have done my best to perform the duties of the office and have felt deeply as each of my predecessors must have felt, that his little service to the College is a very inadequate evidence of his appreciation of the honor which he has received from the College. Among these duties which each President must perform is the delivery of an address at the Convocation. For this he must select an appropriate and interesting topic. In seeking for such a subject I have sought help during the past months and the only suggestions received have all had to do with the very matter which former and wiser Presidents have avoided. Also the College has received a number of letters asking for some statement on this matter. And so for these reasons and to remove the stigma of cowardice from the Presidents of the College, I am tempted to discuss the question " What is an Internist? "

Now we are physicians and doctors and we know what these words mean. Together we are joined to form an American College of Physicians and

* Presidential Address, delivered at the Convocation of the American College of Physicians, Twenty-fourth Annual Session, Cleveland, April 3, 1940.

the meaning of these words is well understood. Perhaps you would think that this should be sufficient and that like the Presidents of past years we might continue to avoid the attempt to define an internist. But we all use this word and we should not do so unless we can justify ourselves. It is not enough for us to say that we know what an internist is, so why bother to define it. Words without a clear meaning should not be used. Perhaps onomatopoetic words need no definition for they repeat the desired sound as, for example, thunder and borborygmus. But even slang has a reason for every word and phrase even though we often fail to know its origin.

And even if we do not admit that we should try to understand the words we use, we should realize how much pleasure we lose if we do not appreciate the origin, derivation and implication of them. Take, for example, the word "sincere." How much meaning it gains when we remember that its origin dates back to the days when if a marble statue was so perfect that there was no crack needing to be filled with wax, it was called *sine cera,* in other words, without wax. So, today, when we sign ourselves "yours sincerely," we mean without any wax, which brings us very close to the modern slang use of the words "soft soap" or "the old oil." I am sure that a clear understanding of all that internist means will likewise lead to a more enjoyable use of the word.

It is science and its followers who should especially be prepared to define accurately its every term, to justify its every word and to be certain that every word has a clear meaning and only one. So it seems that an attempt should be made to define this term "internist," which we all use, even if in making the attempt I prove myself foolhardy. Perhaps the old saying might be paraphrased to read, the novice slashes in where master surgeons fear to cut, and perhaps in the final analysis I shall fail and shall have to claim that like squaring the circle, it just cannot be done. But even if I, personally, did not feel the urge to try this task, it is clearly the duty of the American College of Physicians to define an internist, for Article III of our Constitution refers to our membership as composed of "qualified internists of high standing." Furthermore, our College has decided that all those elected to Associateship from this time on, in order to be eligible for advancement to Fellowship will have to present certification by the American Board of Internal Medicine, which body also has used the term "internist" in its printed folder of information.

So you see the question is an important one to us and faces us on all sides. We cannot laugh it off as we so often do the importunate questions of our patients. We must undertake to find an answer, however inadequate it may be. Certainly it will be some help in disproving the widespread belief of the layman that an internist is the same as an intern. If any of you think that this statement is incredible, let me assure you that it is a fact and further that a recent edition of an authoritative dictionary flatly states that the word internist is a synonym for intern. No doubt it is true that both of these words refer to those doctors who practice within walls but these walls differ;

in one instance being those of the hospital; in the other, those of the body. I am sorry to say we must protest against being confused with interns, however much we envy them their youth and opportunities.

Other dictionaries and the rest of the laity if they have heard the word at all, define an internist as one who practices internal medicine. This may perhaps be as good a definition as is possible but it is certainly inadequate in several directions. In the first place, it merely substitutes one difficulty for another for we lack a satisfactory definition of internal medicine; and secondly, it does not go half far enough.

An attempt to formulate a definition of internal medicine was the text of the Presidential Address by Dr. Reynold Webb Wilcox in 1916 at the first scientific session of the American Congress on Internal Medicine of which our College was a member. He tried to delimit internal medicine by listing twelve categories of disease which together formed its domain, and went on to state that the name internist is undoubtedly the proper one and that an internist is not only a specialist but an expert. We will return to this thought later. Dr. Wilcox went on to say that the American College of Physicians had created an aristocracy among internists, a point of view reiterated by George Vincent in his 1929 address to the College when he called us an elite.

Internist apparently was an acceptable designation twenty-five years ago but is still misunderstood and not in general use throughout our country today. It is amusing to read in the Transactions of that Congress that one of those who discussed the President's Address suggested that a journal be published, to be named "The Internist," which should have as one of its major purposes the equalization of the fees of the surgeon and the internist. Surely this was and is a desirable goal; had it been successful it would have made the word very much more familiar and the internists very much wealthier. Unfortunately the venture was never launched and so neither of these beneficial results was ever reached.

Apparently the term "internist" grew out of the need for a name for the doctor who practices internal medicine and certainly this term "internal medicine" was in use long before the designation "internist" was coined. One can trace the phrase internal medicine far back into the nineteenth century and it would appear to have been used in Germany and France before being adopted in England or in this country. But it was employed with various shades of meaning and it is difficult to find a satisfactory definition of this division of medicine.

One of William Osler's most famous addresses was entitled "Internal Medicine as a Vocation" and all the wisdom of that great essay is as true today as it was in 1897. It should be familiar to all of us and it can be found in that volume of his collected essays which takes its name "Aequanimitas" from the finest of them all. Osler was a very great man but even he does not really define Internal Medicine in that address and expresses the wish, to quote his words "there were another term to designate the wide

field of medical practise which remains after the separation of surgery, midwifery, and gynecology. Not itself a specialty (though it embraces at least half a dozen), its cultivators cannot be called specialists, but bear without reproach the good old name physician, in contradistinction to general practitioners, surgeons, obstetricians and gynecologists."

Nor does Osler trace the history of the origin and growth of internal medicine as distinct from the practice of medicine. This also is difficult to do for its beginnings are hidden in the story of the progress of all medicine. From one point of view it has been done by Prof. Knud Faber of Copenhagen, in 1923, in one of the most fascinating books about internal medicine ever written. It is entitled "Nosography in Modern Internal Medicine," and in it he traces the development of internal medicine as reflected in the constant effort to find a workable classification of disease. Faber divides the history of internal medicine into six parts—first Sydenham and the Nosologists; next the Paris School with its emphasis on anatomic diagnosis. Then followed in order the German school of physiologic medicine, the bacteriologic clinic with Pasteur as its chief exemplar and finally the periods of functional diagnosis and of constitutional pathology. Throughout the book most of the famous figures are referred to as clinicians though many of them would not be so considered today. It is not until Faber refers to Soupault and his observations in 1901 on the symptoms of chronic gastric ulcer that the term internist appears.

In my own opinion the first physician who displayed the point of view which in some ways is the hall mark of the internist, was Sydenham when three centuries ago he turned away from the old confusions of theory without fact to actual observations of fact. This was Sydenham's real contribution and far more important than his oft quoted advice to young students of medicine "Read Don Quixote." That no doubt shows his appreciation of the fact that the physician must know human nature but it might have been better if Sydenham himself had given more attention to the new discoveries of Harvey and of Malpighi which in fact he neglected, although his contemporary Sir Thomas Browne considered Harvey's discovery to be preferred over that of Columbus.

Following him Boerhaave, Bichat, Auenbrugger, Laënnec, Louis, Koch, Graves, Stokes, Corrigan, Bright and Addison, to name only a few, each in his turn laid stones in the growing foundation of Internal Medicine. These men were internists in a measure and were followed by many others on down the list to recent times when only chronologic proximity lessens due recognition. Other famous men whose discoveries made it possible for such a thing as internal medicine to evolve were in no sense internists—Pasteur, Virchow, Claude Bernard. Even Thomas Hodgkin who was a physician was not really an internist.

Long before internal medicine had appeared surgery had become a separate specialized branch of medicine, obviously because of the fact that anatomy, so essential for surgery, was the first of what we term today the basic

sciences, to supply a body of information beyond the ability of assimilation of the general practitioner. Also the need of special manual ability hastened the flowering of surgery. Internal Medicine had to wait until the accumulation of knowledge of physical diagnosis, clinical medicine and of therapy had had added to it the basic facts of physiology, bacteriology, biochemistry and pharmacology to form a body of knowledge requiring the full attention of anyone who would be familiar with it all.

This is the mechanism which acts to split branches and specialties off the main trunk. It is not a decision but an evolution. When the mass of information and of technic grows so large that it can no longer be included in the general knowledge of the practitioner then it is allotted to that certain group who willingly learn this at the cost of all else. It is as inevitable as evolution and cannot fail; but, on the other hand, hasty attempts to anticipate the process on the basis of inadequate aggregates of specialized knowledge are equally certain of failure. Internal Medicine came about properly and in due course, and as a further step in the same direction came into being this group of individuals who are, in the first place, physicians, next practitioners of internal medicine and finally internists.

So now we come back to our starting point—the name internist. It is not such a new word as some might think nor is it so clearly understood or widely adopted as others would believe. In various parts of this country it is scarcely known at all and such terms as diagnostician, medical consultant or even clinician are applied to that individual who elsewhere would answer to the name internist. None of these other terms is as satisfactory for this purpose; diagnostician excludes therapy which is an inherent function of the internist; nor should the internist be thought of as one who sees patients only in consultation. In no way can an internist better exhibit his skill than in the personal physician to patient relationship. There is even less excuse for the use of the word "clinician" in this connection. Internist is the best term even though it has not established itself as yet.

It is hard to trace its very beginnings. Undoubtedly it was used in France and Germany before coming to this country. I cannot find it in the Index Catalogue of the Library of the Surgeon General nor in any of Osler's many essays, nor as I have already said, do the dictionaries help us. Apparently it stemmed from internal medicine and if it had originated in England or here might just as well have been internalist as internist. In fact, some dictionaries define an internist as one treating only the diseases of the internal organs. But it came from the French "interniste" instead.

This is the background of our problem and it is easy to see two reasons why a satisfactory definition has not, and perhaps never will, be put into words. The first of these arises from the fact that the word we are trying to define is derived from the term "internal medicine," which in turn is undefinable and which in the very nature of things is changing its meaning from decade to decade. Its borders are not fixed; it is not a mere matter of internal and external medicine. What at one epoch may belong to the

domain of internal medicine may shortly be excluded and on the other hand, the advance of science may bring new or return old, divisions of knowledge to its fold. Clearly if internal medicine cannot be better defined then the exponent of this field, the internist, can only be described in terms of the field itself.

In the second place, our difficulty depends upon the inherent nature of a definition. All that a definition can do is to define and to delimit; it is a flat statement of the basic meaning of a word as determined by derivation and usage. A definition is static and dead. Internal medicine and the internist are neither static nor dead and never will be. Nor will all the full meaning of these words ever be included in any definition. But let us state a definition for better or worse, and then let us consider what any such definition will inevitably fail to express. It must be worded somewhat in this fashion:

An internist is a physician fitted by a sound and applicable knowledge of the basic sciences, a continuing training in clinical medicine, a familiarity with fields outside his own, and an intellectual rather than a manual or technical approach, to study, diagnose and treat the diseases of the field of internal medicine to which he strictly limits himself and to integrate with the knowledge of his own field that of the allied specialties.

This may be far from satisfactory but it comes as near to telling the truth and nothing but the truth as I have been able to make it. But does it tell the whole truth? By no means! For to us the word "internist" has a far wider meaning than that which can be encompassed by any definition. Through use the word has gained and grown until today it is a living thing with secondary accessory implications—heard like the overtones of a musical chord. The student of harmonics can define the note C or a given chord and can also recognize but cannot accurately define the many overtones which only the trained ear can hear. But the enumeration of the overtones of the word "internist" is a still more difficult matter.

Let me describe what I hear in this word "internist":

An internist is, of necessity, a physician of exceptional training for his is the field of greatest width. He must have served his apprenticeship years acquiring information, then slowly transformed that essential but relatively base metal into precious knowledge and still unsatisfied, devoted his maturer efforts to the transmutation of knowledge into priceless wisdom.

An internist is one who with sufficient foresight has been willing to pass through what Sir Andrew Clark termed the ten years of dry bread, and the ten years of bread and butter, in order to reach the final twenty years of cakes and ale. He is one who has followed Osler's admonition "Let him not lose the substance of ultimate success in grasping at the shadow of present opportunity."

Being an internist is a state of mind. It implies a breadth of interest which inherently excludes narrow specialism. It demands a vital interest in

medicine of the past, of the present, and as far as possible of the future. The true internist is an " ingenious man " in the old sense of that word, when it was properly used to indicate an active intellectual inquiring mind. The highest praise that Samuel Pepys could give was—" He was an ingenious man." Our internist is of such a nature and his interest in science extends beyond medicine proper, without loss of sympathy with the suffering individual.

Interest in many fields of human thought must be a characteristic of every internist, for humanity and all its doings fascinate him. Culture in its true sense of simple appreciation of the fine products of human skill, art and endeavor belongs to such a nature. Similarly a high moral code and strict ethics are essential ingredients in this picture which we are sketching. Intellectual courage and high standards of duty to his work, to his patients and to his community are inherent to his personality.

These are a few of the overtones and implications which I hear in this word " internist." Each of us has known some such individuals, each of us has some exemplar upon whom we would model ourselves. He may have been some outstanding historical figure such as those we have named or he may be some humbler or more recent figure not yet known to fame but if he be an internist with all that this term implies, he is without doubt the highest type of the physician which evolution has produced.

We like to think that our College is composed of individuals who possess in great measure all these qualities which the term " Internist " implies. We pride ourselves that our Fellows are seeking to achieve such high goals.

You, newly elected members, are admitted to the College because in you are recognized the potentialities, the material and the spark necessary to make you achieve the stature of the ideal internist. See to it that you gain inspiration from being a part of this great College and that in turn you add to its glory by your own efforts and success in making of yourself an internist. If this conception of what it means to be an internist is true, then your task is no easy one but the challenge of difficulty is a strong stimulant and the laurels of success are to be gained in many directions besides those of the material rewards of this world.

I hold very strongly that the internist should not be too narrowly specialized within the field of Internal Medicine. On the contrary, he should be highly specialized in Internal Medicine and if, for any reason, he becomes particularly interested in one or another sub-division of this field, he must, to retain the title " Internist " in its full sense, continue his familiarity with the whole domain of Internal Medicine. If I read the signs of the times correctly, the need today is for more true internists rather than for more internists who have become specialized in limited sub-branches. The field is open for the well-trained internist and I hope that more and more of the members of this College will qualify themselves for this high task.

Nothing that you are being asked to be or to do is new or peculiar to the internist, but perhaps as internists you should exhibit these qualities in

the highest degree. The principles involved almost antedate medical history, you will hear them tonight in the Oath of Hippocrates and you will find them in that other still older Oath of the Hindu Physician. "Devote yourself to the healing of the sick even if your life be lost by your work." "Do the sick no harm." "Always seek to grow in knowledge."

And now let me draw two conclusions from what has been said: first, that if our delineation of an internist is a true one, then our College must reword its Constitution for how can it refer to "highly qualified internists" when there can be no such creature as an unqualified internist. If he be not in all things excellent, then let him not be termed an internist.

Secondly, that if this brief characterization of an internist be the truth, it is obvious at once that never will it be included in a definition. We see at once why no President has ever offered a satisfactory definition and why no one ever will. The subject is an endless one and it might become the repeated topic of many annual convocational addresses without fear of repetition in the same fashion as the ever old but ever new, annual lectures on "The Care of the Patient" at Harvard.

Personally, I find some comfort in the classical story of the brilliant Greek poet Simonides who when Hieron challenged him to define the nature and attributes of God asked for a day's time to prepare his answer, and the next day begged for two days more, and on each occasion doubled the period that he required for thought. When at last Hieron demanded an explanation, Simonides replied that the longer he pondered the matter, the more obscure it became. And that is where the matter of a definition of an internist rests for all of me.

And now in closing let me leave this thought with you. It is of the very essence of life that it should be impossible to define certain things. An internist is such an undefinable entity and this is as it should be. To be defined he must be standardized, and if he be standardized then even if he be all that we have added unto him yet shall he fail—for with standardization dominant, no one, internist or otherwise, can be what he needs to be to be above all else —himself—an individual—a man.

FUNCTIONAL AORTIC INSUFFICIENCY *

By CURTIS F. GARVIN, M.D., *Cleveland, Ohio*

ORGANIC aortic insufficiency has been recognized since Cowper [1] first described this condition anatomically in 1706. The physiological changes attracted attention in 1715 when Vieussens [2] noted the collapsing pulse. Further important diagnostic signs were recorded by Hope [3] in 1831.

The observations of Corrigan [4] in 1832 concerning the mode of origin, meaning and character of the auscultatory and palpatory phenomena of aortic insufficiency stimulated interest in the condition and thereafter the literature increased steadily. Relative aortic insufficiency came to be recognized, and in 1896 Barié,[5] in an article entitled "True and False Aortic Insufficiency," made a comprehensive review of the contributions to that date.

Subsequently numerous observers have reaffirmed the association of aortic dilatation and relative aortic insufficiency with chronic hypertension or granular kidneys. These reports have tended to indicate that the occurrence of the condition is rare.

The present communication indicates that relative aortic insufficiency is more frequent and more important than is generally supposed. Two hundred consecutive autopsied cases of hypertensive heart disease were studied and 14 instances of relative aortic insufficiency were discovered, an incidence of 7 per cent. All of these cases were seen on the medical divisions of Cleveland City Hospital, and although in some instances there was a difference of opinion as to the significance of the aortic diastolic murmur there was no question as to its existence. The importance of the lesion is apparent when one considers that in several instances it led to frank errors in diagnosis. The salient details of these cases are noted in the following case reports.

CASE REPORTS

Case 1. A. F., a 65-year-old white male, had had symptoms of myocardial insufficiency for one year. On examination three observers heard a prolonged low-pitched loud diastolic murmur to the right and left of the sternum in the second and third interspaces. The cardiac conduction mechanism was normal. The blood pressure was 210 millimeters of mercury systolic and 110 diastolic. The patient died on the second hospital day. The clinical diagnosis was syphilitic aortic insufficiency and myocardial insufficiency.

The autopsy showed evidence of chronic myocardial insufficiency. The heart weighed 700 grams. All the heart valves were normal. The aortic valve ring measured 7.5 cm., normal for a male of this age being 8.03 cm., according to Roessle.[6] The pericardium was not adherent, the coronary arteries showed moderate to marked sclerosis, and there was generalized arterial and arteriolar sclerosis. The final diag-

* Received for publication August 17, 1938.

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nosis was generalized arterial and arteriolar sclerosis, coronary artery sclerosis, myocardial fibrosis, cardiac hypertrophy and dilatation, and myocardial insufficiency.

Case 2. W. C., a 63-year-old colored male, had had symptoms of myocardial insufficiency for two years. Examination showed a soft diastolic murmur at the aortic area. The murmur was inconstant. The cardiac conduction mechanism was normal. The blood pressure averaged 160 millimeters of mercury systolic and 110 diastolic. The Wassermann test was negative. The patient died on the one hundred twenty-eighth hospital day. The clinical diagnosis was hypertensive heart disease, the diastolic murmur being considered insignificant.

The autopsy showed a dilated heart weighing 450 grams, coronary sclerosis, and generalized arterial and arteriolar sclerosis. All the heart valves were normal. The aortic valve ring measured 8.5 cm., average normal for this age and sex being 8.03 cm. The final diagnosis was as in Case 1.

Case 3. E. P., a 35-year-old colored male, had had symptoms of cardiac failure for six months. He had had a chancre 13 years previously. Seven observers agreed as to the presence of a to-and-fro murmur heard best at the aortic area and to the left of the sternum but also at the apex. The cardiac conduction mechanism was normal and there was a gallop rhythm. The blood pressure was 150 millimeters of mercury systolic and 110 diastolic. The Wassermann test was four plus. The patient died on the one hundred forty-sixth hospital day. Because the murmur was not constant, most of the clinical observers believed this to be hypertensive heart disease with a functional aortic insufficiency, although the possibility of luetic aortic insufficiency was considered.

The autopsy showed typical findings of hypertensive heart disease with failure. The heart was dilated and weighed 650 grams. All the valves were completely normal. The aortic valve ring measured 9 cm., the normal value for a patient of this age and sex being 6.46 cm.

Case 4. A. B., a 53-year-old colored female, had had symptoms of cardiac failure for 13 months. On examination five observers heard a loud diastolic and a softer systolic murmur over the upper chest. The cardiac conduction mechanism was normal. The blood pressure was 180 millimeters of mercury systolic and 60 diastolic. The Wassermann test was negative. The patient died on the twenty-fourth hospital day. The clinical diagnosis was syphilitic aortic insufficiency and heart failure.

At postmortem examination the heart was dilated and weighed 575 grams. There was generalized arterial and arteriolar sclerosis. The valves were normal. The aortic valve ring measured 9 cm., the normal for a patient of this age and sex being 7.09 cm. The final diagnosis was hypertensive heart disease with cardiac failure.

Case 5. J. E., a 59 year old colored male, had had symptoms of myocardial insufficiency for three years. According to four observers there was a loud to-and-fro murmur at the aortic area. The cardiac rhythm was auricular fibrillation. The blood pressure could not be determined exactly but was considered to be 150 millimeters of mercury systolic and 50 diastolic. The Wassermann test was negative. The patient died on the day of admission. The clinical diagnosis was syphilitic aortic insufficiency with heart failure.

At postmortem examination the heart was dilated and weighed 650 grams. The valves were normal. The aortic valve ring measured 8 cm., the normal value for this sex and age being 7.77 cm. There was moderately severe coronary sclerosis. The final diagnosis was as in Case 1.

Case 6. E. W., a 41-year-old colored female, had had symptoms of myocardial insufficiency for one year. A diastolic aortic murmur of medium intensity was heard by six different examiners. The cardiac conduction mechanism was normal and the blood pressure was 220 millimeters of mercury systolic and 98 diastolic. The Wassermann test was negative. The clinical diagnosis was syphilitic aortic insufficiency and heart failure.

At postmortem examination the heart was dilated and weighed 525 grams. The valves were normal and the aortic valve ring measured 6.5 cm., normal being 6.8 cm. The final diagnosis was as in Case 1.

Case 7. W. K., a 50-year-old colored man, had had symptoms of myocardial insufficiency for two years. Four observers agreed to the presence of a to-and-fro murmur, with the diastolic element loudest at the aortic area. The blood pressure on admission was 170 millimeters of mercury systolic and 90 diastolic, and this subsequently fell to 110 systolic and 80 diastolic. Coincident with this the diastolic murmur disappeared. The Wassermann test was four plus. The patient died on the one hundred first hospital day. On admission the clinical diagnosis was syphilitic aortic insufficiency, but when the murmur disappeared the diagnosis was altered to cardiac hypertrophy and failure with incidental luetic aortitis.

The autopsy showed the heart to weigh 475 grams and to be dilated. The valves were normal and the aortic valve ring measured 9 cm., normal being 6.95 cm. There was a luetic aortitis without dilatation of the aorta, narrowing of the coronary ostia or extension to the aortic valve. The cause of the cardiac hypertrophy and cardiac failure was obscure. The final diagnosis was cardiac hypertrophy and failure.

Case 8. D. Y., a 44-year-old colored male, had had symptoms of cardiac insufficiency for one year. Five examiners heard a diastolic murmur at all areas, loudest at the aortic. The cardiac conduction mechanism was normal. The blood pressure was 210 millimeters of mercury systolic and 120 diastolic. The Wassermann test was four plus. The patient died on the twenty-fifth hospital day. The clinical diagnosis was hypertensive heart disease with heart failure and relative aortic insufficiency due to cardiac dilatation.

At postmortem examination the heart was dilated and weighed 700 grams. The valves were normal. The aortic valve ring measured 8 cm., normal being 6.95 cm. There was an uncomplicated syphilitic aortitis. Generalized arteriolar sclerosis was present. The final diagnosis was hypertensive heart disease with cardiac failure, and syphilitic aortitis.

Case 9. L. J., a 45-year-old colored female, had had symptoms of myocardial insufficiency for six months. Four observers heard a to-and-fro murmur at the aortic area and to the left of the sternum. The cardiac conduction mechanism was normal. The blood pressure was 130 millimeters of mercury systolic and 100 diastolic. The Wassermann test was four plus. The patient died on the seventy-eighth hospital day. The clinical diagnosis was syphilitic aortic insufficiency with cardiac failure.

The autopsy showed a dilated heart weighing 375 grams. The valves were normal and the aortic valve ring measured 8 cm., normal being 6.8 cm. There was no syphilis of either the aorta or the aortic valve. The final diagnosis was as in Case 3.

Case 10. J. D., a 58-year-old colored male, had had symptoms of myocardial insufficiency for six months. Four examiners heard a to-and-fro aortic murmur. The cardiac conduction mechanism was normal and the blood pressure was 160 systolic and 100 diastolic. The Wassermann test was negative. The patient died on the thirty-fourth hospital day. The clinical diagnosis was syphilitic aortic insufficiency and heart failure.

The autopsy showed a dilated heart weighing 460 grams. The valves were normal and the aortic valve ring measured 8.5 cm., the normal being 7.77 cm. There was no syphilitic aortitis. The final diagnosis was as in Case 3.

Case 11. G. C., a 62-year-old colored male, had had symptoms of myocardial insufficiency for one month. There was a history of lues with inadequate treatment. Four examiners heard a short diastolic murmur to the left of the sternum. The cardiac conduction mechanism was normal. The blood pressure was 210 millimeters of mercury systolic and 138 diastolic. The Wassermann test was negative. The clinical diagnosis was hypertensive heart disease. The aortic insufficiency was variously considered to be due to either sclerosis or syphilis.

At postmortem examination the heart was dilated and weighed 550 grams. The valves were normal. The aortic valve ring measured 8 cm., normal being 8.03 cm. There was marked arterial and arteriolar sclerosis. There was no syphilitic aortitis. The final diagnosis was as in Case 3.

Case 12. W. D., a 78-year-old colored male, had had symptoms of myocardial insufficiency for eight months. Four examiners heard a loud diastolic aortic murmur. The blood pressure was 190 millimeters of mercury systolic and 70 diastolic and the cardiac conduction mechanism was normal. The Wassermann test was negative. The aortic insufficiency was considered to be organic, probably due to sclerosis.

The autopsy showed a dilated heart weighing 625 grams. The heart valves were normal and the aortic valve ring measured 9 cm., normal being 8.2 cm. The final diagnosis was as in Case 1.

Case 13. T. K., a 38-year-old white female, had a two year history of myocardial insufficiency. Six observers heard a to-and-fro aortic murmur from time to time. The blood pressure was 250 millimeters of mercury systolic and 160 diastolic. The cardiac conduction mechanism was normal. The Wassermann test was negative. The patient died on the forty-eighth hospital day. The clinical diagnosis was hypertensive heart disease. The murmur was variously ascribed to rheumatic valvulitis or ring dilatation.

The autopsy showed a dilated heart weighing 450 grams. The valves were normal. The aortic valve ring measured 6.5 cm., normal being 5.73 cm. There was severe vascular disease and nephrosclerosis. The final diagnosis was as in Case 3.

Case 14. E. B., a 68-year-old colored female, had had symptoms of myocardial insufficiency for 18 months. Three examiners heard a moderately loud aortic diastolic murmur which subsequently disappeared. The blood pressure was 210 millimeters of mercury systolic and 100 diastolic. The cardiac rhythm was auricular fibrillation. The Wassermann test was negative. The clinical diagnosis was hypertensive heart disease.

At postmortem examination the heart was dilated and weighed 510 grams. The valves were normal. The aortic valve ring measured 10 cm., normal for this age and sex being 7.65 cm. The final diagnosis was as in Case 3.

Comment

It will be noted that in the majority of these cases the murmur was loud and easily heard so that there need be no doubt concerning its presence. Furthermore, in most instances four or more observers agreed to its existence. The wide pulse pressure (averaging 85 millimeters of mercury) is confirmatory evidence of an aortic leak. This is in contrast to the fact that the pulse pressure in the 186 cases of hypertensive heart disease without aortic insufficiency averaged 65 mm. of mercury.

The clinical interpretation of these murmurs is interesting. In Cases 1, 4, 5, 6, 9 and 10 the aortic insufficiency so predominated the picture that an outright diagnosis of syphilitic heart disease was made. In Cases 3, 11 and 12 it could not be decided whether the murmur was due to syphilitic aortic valvulitis or sclerosis of the valves. In Case 13 the murmur was considered to be characteristic of aortic insufficiency and was variously thought to be due to rheumatic valvulitis or dilatation. The working impression in Cases 2 and 7 was syphilitic aortic insufficiency, but in these two cases the murmur disappeared so that the final diagnosis was hypertensive heart dis-

ease. In Case 14 an initial impression of arteriosclerotic aortic insufficiency was abandoned when the murmur proved to be transient. The correct diagnosis of functional aortic insufficiency was made in Case 8.

Although the series is small, the high incidence of colored patients is striking, i.e., 12 out of 14 (86 per cent). This is in contrast to the fact that in the 186 cases of hypertensive heart disease without aortic insufficiency there were 66 colored patients (35 per cent). The percentage of males and females was practically the same in the cases with and without murmurs.

The autopsies in these cases showed a rather constant picture: evidence of severe myocardial insufficiency, marked cardiac dilatation and normal heart valves with special emphasis on the fact that the aortic valve showed no anatomical abnormalities. The aortic valve ring in these 14 cases averaged 8.25 cm. in circumference, whereas the average of the normal values for these cases is 7.3 cm. None of the cases showed pericardial adhesions. Cases 7 and 8 had syphilitic aortitis but there was no dilatation of the aorta and no aortic valvulitis. There was rather uniform anatomical evidence of hypertension in the way of generalized arteriolar sclerosis and arteriolar nephrosclerosis. The pathological findings clearly indicated that the aortic insufficiency noted in life was functional and not due to anatomical changes in the valve leaflets.

In a personal communication to the author Dr. R. W. Scott has described the case of a 17-year-old boy who was the victim of malignant hypertension. This patient, even when his circulation was compensated, had a characteristic murmur of aortic insufficiency. By administering amyl nitrite, the blood pressure could be temporarily lowered, the diastolic aortic murmur would disappear, and the second sound would become tambouric and clear. Whether this will aid in the differential diagnosis of functional and organic aortic murmurs in the face of the severe dilatation of heart failure remains to be seen.

Summary

A survey of 200 consecutive autopsied cases of hypertensive heart disease discloses 14 cases in which a diastolic murmur was heard at the base of the heart. This finding led to varying degrees of difficulty in clinical interpretation. In four instances a frank error in etiological diagnosis was made. At autopsy the heart in these cases was dilated but showed perfectly normal valves. In fact, the pathological findings permitted no other conclusion than that the aortic insufficiency noted in life was functional and not due to anatomical changes in the valve leaflets.

It is thought that functional aortic insufficiency occurring in cases of hypertensive heart disease is more common and more important than is generally recognized.

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PRESENT STATUS OF THE PULPLESS TOOTH *

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The status of the pulpless tooth has undergone a definite change in the last few years. Reëducation of the physician, as well as the dentist, on this point is both necessary and timely. It will, therefore, be the object of this paper to define the pulpless tooth and interpret the facts concerning it in the light of recent studies.

At the outset it must be made clear that periapical infection can, and sometimes does, cause infection elsewhere in the body. The frequency with which such foci of infection exist and cause systemic disease is open to question, however, and has without doubt been greatly overemphasized in the past. The author is in agreement with the following statement of Billings,[1] who did so much to place the concept of focal infection before the medical profession: "Focal infection as a cause of disease has come to stay. But, like every other principle in medicine, it has its limitations."

Experimental evidence, as well as clinical observation, of the relationship of dental foci of infection to systemic disease is not lacking. Rosenow and Meisser [2] have experimentally produced renal calculi in dogs by removing the pulps of teeth and sealing streptococci in the root canals. Following a somewhat similar technic Jones and Newsom [3] succeeded in producing myocardial changes in dogs, e.g., vegetative or verrucose lesions in the region of the mitral or aortic valves, parenchymatous degeneration, and round cell infiltration. The dogs became fatigued more easily than normal controls, and presented symptoms somewhat similar to those generally associated with heart disease in the human. Haden [4] produced peptic ulcers in dogs by injecting a culture prepared from bacteria recovered from the roots of infected teeth of patients suffering from peptic ulcers.

In addition to the few experimental studies cited here, numerous clinical case reports would seem to attest to the validity of the focal infection theory. Bierring [5] has recently reviewed the more important literature dealing with focal infection, and an excellent summary of the status of oral focal infection is given by MacNevin and Vaughn.[6] It is not the purpose of this paper to question the validity of the focal infection concept. It is only desired to point out that, on the basis of recent studies, focal infection from pulpless teeth occurs less often than was previously thought. It must be emphasized also that although a focus of infection may be present, e.g., around the root apices of certain pulpless teeth, it does not follow that focal infection is also present. The latter term implies systemic dissemination from the focus.

* Received for publication September 13, 1939.

Misconceptions Concerning the Pulpless Tooth

It is desired first to clear up two popular misconceptions regarding the pulpless tooth. Since 1910 it has been the general opinion of many physicians and dentists alike, (1) that a pulpless tooth is a "dead" tooth, and (2) that Hunter[7] aimed his shaft of criticism against the pulpless tooth.

A pulpless tooth is not a dead tooth. It still has a definite and vital relationship with the surrounding tissue. Because of the peculiar anatomic and structural make-up of the dental tissues, the erroneous concept of a "dead" tooth gained currency. Actually, the life of the tooth depends upon its attachment apparatus, i.e., periodontal membrane and adnexa. In the words of Marshall[8]: "The life of the tooth is dependent upon the integrity of the periodontal membrane and not upon the integrity of the pulp." As a matter of fact, many embryologists believe that the function of the pulp ceases when the tooth is completely calcified, shortly after eruption. If a pulpless tooth were a dead tooth, it should be exfoliated, since the body seldom tolerates dead tissue. That a pulpless tooth is not dead may be evidenced by the pain experienced upon its removal without an anesthetic.

In his history-making address in Montreal in 1910, Hunter[7] did not refer specifically to the pulpless tooth as a source of oral sepsis when he condemned the kind of dentistry then prevalent. How the pulpless tooth came to be maligned instead of the accumulation of filth around ill-fitting crowns and bridge-work, against which Hunter inveighed, will probably never be known. The entire matter is summed up in a much overlooked but important editorial[9] in the *Journal of the American Dental Association.* The editor referred to Hunter's criticism as follows: "The 'oral sepsis' of which he complains, and not without reason—had nothing whatever to do with the thing that, during the decade that followed his address, caused the greatest concern among the profession, i.e., focal infection from apical ends of pulpless teeth. This is the thing that claimed our major consideration, and in connection therewith the name of Hunter has repeatedly been quoted. As a matter of fact, Hunter never referred in the remotest way to the evils of pulpless teeth as such. He was concerned with the sepsis that came from accumulations around crowns, bridges, and artificial dentures, calling them 'gold traps of sepsis.' . . . Mayhap if this distinguished scientist had given his whole-hearted attention to this important question, the mental aberration and almost universal prejudice against the pulpless tooth that has developed might have thereby to a certain degree been avoided." That this misconception could have been perpetuated for so many years is indicative of the hysterical era which followed Hunter's criticism. Had his words been taken literally, the orgy of extraction, that continued for more than two decades, might have been averted.

Studies bearing on the pulpless tooth as a possible focus of infection may be divided into: I, clinical; II, roentgenologic; III, histologic; IV, bacteriologic. Only the more important findings in each group will be discussed here.

I. Clinical Studies

1. It is a well known fact that a large number of people having pulpless teeth show no apparent systemic involvement. It is also significant, perhaps, that no definitely conclusive proof has yet been advanced that, in any case, a tooth or teeth were the direct cause of the systemic disturbance, excepting a priori proof. The extraction of a tooth followed by amelioration of symptoms does not necessarily prove that the tooth was the cause of the disease. This is only an assumption which may or may not be true.

2. During the World War draft, data were collected of more than two and one-half million men between the ages of 18 and 30 years. An evaluation of the data, according to Appleton,[10] shows that "chronic infection about the head is not . . . the sole determining factor in the contemporaneous occurrence of such conditions as gastric ulcer, appendicitis, endocarditis, arthritis, osteitis deformans, myositis, and muscular rheumatism."

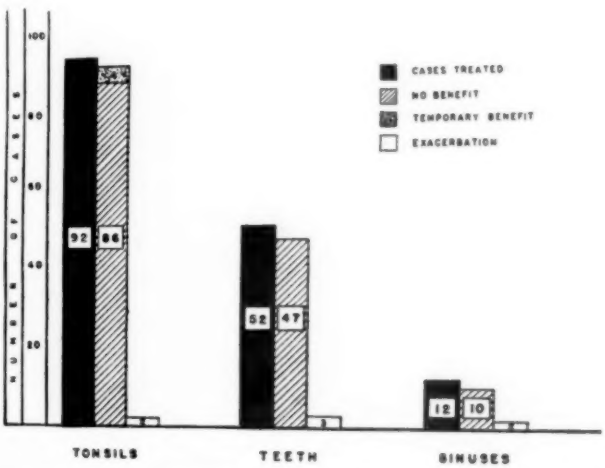

Fig. 1. The results of treatment of tonsils, teeth and sinuses in a group of 200 patients with rheumatoid arthritis (Cecil and Angevine: Ann. Int. Med., 1938, xii, 577).

3. Frankel[11] studied the incidence of systemic disturbances in a large group of people with and without so-called "heavy dentistry." By this term he meant the presence of crowns, bridges, pulpless teeth and any other dental evidence which might suggest the presence of a focus of infection. He concluded that the incidence of systemic disturbances in the "heavy dentistry" group was not materially higher than in the other group.

4. Cecil and Angevine[12] recently analyzed the results of the elimination of foci of infection in 200 cases of rheumatoid arthritis. They came to the conclusion that no benefit accrued to 47 out of 52 patients for whom dental foci of infection were removed (figure 1).

II. Roentgenologic Studies

1. Full mouth roentgen-ray pictures of more than 1500 patients were studied by Ziskin[13] to determine whether a direct correlation existed between positive roentgen-ray findings of pulpless teeth and systemic disturbances. The subjects were patients in the wards of a city hospital, from the out-patient department of the same hospital, and ambulants who applied only for dental treatment and who were well otherwise. Ward and outpatient subjects were examined by the medical staff and complete medical histories were available. The following is a synopsis of the study: (*a*) 48 per cent of the subjects studied were sick, 52 per cent were well; (*b*) 71 per cent of the "sick" group and 75 per cent of the "well" group had pulpless teeth; (*c*) of those with pulpless teeth, 46 per cent were sick and 54 per cent were well, whereas of those without pulpless teeth, 50 per cent were sick and 50 per cent were well. From these findings it is obvious that a relationship between pulpless teeth and systemic disease in the groups studied is certainly not striking.

2. Arnett and Ennis[14] made complete routine medical and dental examinations of 883 college students, including complete roentgenologic studies of the teeth. Although 19.8 per cent of the group had periapical areas of rarefaction, no statistically significant association with systemic disease could be demonstrated. The areas of rarefaction were not associated with rheumatism, chorea, or heart disease. From a review of the literature and upon the basis of their own study, the authors conclude that: "The wholesale removal of devitalized teeth and teeth with granulomata is certainly without justification in healthy young individuals."

III. Histologic Studies

Histologists who have studied sections of pulpless teeth are agreed, almost without exception, upon three things: (1) that periapical bone restoration can and often does follow satisfactory root canal treatment of pulpless teeth; (2) that such pulpless teeth are commonly without histologic evidence of infection; and (3) that they may be safely retained in the mouth. It is interesting also to note that of 250 roentgen-ray negative pulpless teeth, Skillen[15] found evidence of infection in only six upon histologic examination.

IV. Bacteriologic Studies

The most indicting evidence against the pulpless tooth as a focus of infection has come from the bacteriologic laboratory. The two outstanding studies in the field of dental focal infection, considering both the quantity and quality of material studied, are probably those of Haden[16] and of Burket.[17] The data are particularly valuable for comparative analysis because Haden used one method of study and Burket another. Burket used the "external approach" method, which consisted in aseptically laying bare the alveolar tissues and making a culture direct from the root apex while the tooth was still in situ. Haden first extracted the tooth and then made

cultures from the root end. Burket reported results on 429 teeth, and Haden on 1500 teeth. Haden obtained growth from 87 per cent of pulpless teeth and from 55 per cent of vital teeth; Burket obtained growth from 72 per cent of pulpless teeth and 43 per cent of vital teeth. These findings run fairly close together considering the fact that the methods differed and the material was not identical. This important observation may now be made: If the vital teeth are used as controls, the difference between the percentages of growth found in the pulpless and in the vital teeth will then give us the actual percentage of growth found in pulpless teeth (see figure 2). Since,

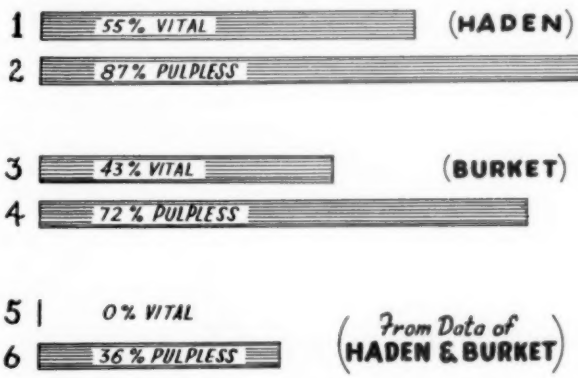

FIG. 2. (1–4) Per cent of growth from vital and from pulpless teeth obtained by Haden and by Burket. When per cent of growth from vital teeth (5) is taken as normal, the growth from pulpless teeth (6) is only 36 per cent.

in the combined data of Haden and Burket, the weighted average for growth from pulpless teeth is 85 per cent, and the weighted average for growth from vital teeth is 49 per cent, the difference, or 36 per cent, is probably nearer the *actual* percentage of growth found in pulpless teeth. If we add to this the fact that the pulpless teeth studied by Haden and Burket were treated a number of years ago, when root canal therapy was not so satisfactory as it is today, and that the finding of bacterial growth in cultures from teeth does not necessarily imply the presence of infection, the bacteriologic evidence against the pulpless tooth is not so damning.

RECENT INVESTIGATIONS

A new interpretation of past studies on the pulpless tooth must be given in the light of recent studies by Fish and MacLean,[18] Okell and Elliot,[19] and Gunter and Appleton.[20] These studies practically compel one to scrap all previous bacteriologic studies dealing with pulpless teeth.

An important study, destined to have a far-reaching influence upon the interpretation of the bacteriologic status of pulpless teeth, was reported by Fish and MacLean [18] in 1936. They had made the observation that, despite the fact that a great many investigators recovered bacteria from living pulps, both the pulps and periapical tissues of vital, healthy teeth were invariably

free of any evidence of bacteria or irritation when examined histologically. They therefore wondered whether the microörganisms gained access to the pulp during extraction and arrived too late to set up a reaction. This supposition was strengthened by a study reported by Okell and Elliot,[19] who recovered mouth organisms from circulating blood within a few minutes after extraction of a pyorrheic tooth, even though the blood was sterile immediately before and again some time after the extraction. Apparently sufficient trauma was present during the act of extraction to force organisms into the blood stream, there to produce a transient bacteremia. The question then arose as to whether these organisms were present in the periapical tissues before extraction or whether they came from the pyorrheic pocket. They reasoned as follows: "If our view were correct, provided we sterilized the pocket before extraction, we should always get a sterile apex, a sterile pulp and sterile blood stream after extraction; but if we were wrong and if the organisms were indeed living freely among the cells in the periapical tissues and in the pulp, our sterilization of the pocket would make no difference and after extraction we should still find the apex and the pulp infected and the patient would have the usual transient bacteremia which Okell and Elliot had discovered, and which we had ourselves confirmed." This question Fish and MacLean set out to settle, and found that the organisms came from the debris in the pyorrheic pocket despite attempts to sterilize the pocket by means of antiseptics. Only when the pocket was cauterized with a red hot cautery did they succeed in preventing a transient bacteremia. They thus proved that bacteria were "pumped" into the blood and lymph channels during manipulation of the tooth while it was being extracted. They found further that streptococci are present only in necrotic areas of bone and do not diffuse through the granulation tissue (if it be present) about the root apex. Such streptococci are only transient migrants in the environment of living tissue and require necrotic material in which to grow. In grossly infected pulpless teeth the infection is limited to the root canals or can be found in the pus of the associated abscess. Even in such cases the neighboring alveolar bone and soft tissues are sterile, although they may be irritated by the diffusion of toxic products. The importance of the work of Fish and MacLean lies in the fact that they have shown that it is practically impossible to remove a tooth aseptically (without actual cauterization of the gingival crevice) because bacteria are forced into the pulp and periapical tissues during the act of extraction.

Experimental evidence that bacteria are capable of being "pumped" into a tooth during extraction is given by Kanner,[21] who attempted to copy in vitro the mechanism of pumping or sucking bacteria into pulps of extracted teeth by way of the apical foramen. The method consisted of placing a freshly extracted tooth into a lateral bulge or pocket blown in a test tube. In the bottom of the tube was a suspension of *B. sporogenes,* an easily identifiable organism. The tube was connected to a vacuum pump and the pressure was lowered to about one-half atmosphere. The tube was then

tilted so that the tooth dropped into the bacterial suspension and the atmospheric pressure was then restored to normal. The tooth was removed from the tube, the surface cleansed mechanically, sterilized after the method of Tunnicliff and Hammond,[22] then placed in nutrient gelatin and incubated under anaerobic conditions. In all cases in which the bacterial suspension had been "pumped" into the pulp the same organism grew out of the apical foramen. In addition, histologic sections showed the presence of these organisms within the pulps of the "pumped" teeth. From these experiments Kanner concluded that pressure (or suction) is capable of causing bacteria to enter the pulp and that such a mechanism may be operative during extraction, particularly during luxation of the tooth from its socket when spaces are opened up which are capable of admitting microörganisms from the neighborhood.

Evidence that even the best bacteriological technic cannot prevent the risk of contamination during extraction is further given by Tunnicliff and Hammond [22] who found streptococci in the pulps of intact, vital teeth even after adequate surface sterilization. Their method was as follows: Teeth were placed in 88 per cent phenol for 15 minutes, washed in alcohol, flamed, left in alcohol for 15 minutes and flamed again. The teeth were then cultured for eight days in glucose-brain broth to determine sterility. Thirty teeth showing no surface growth were then opened aseptically, and smears, sections and cultures of the pulp were made. In 10 cases growth was obtained even though the teeth used in the study were externally intact and sterile. Histologic sections of the pulps showed no signs of infection, and Tunnicliff and Hammond concluded from this study that their "findings are in accord with those of Fish and MacLean that, histologically, streptococci may be demonstrated in pulps of intact teeth without any evidence of infection."

Indirectly supporting the work of Fish and MacLean are the studies of Okell and Elliot,[19] and of Burket and Burn.[23] As has already been mentioned, Okell and Elliot took blood cultures before, and then 10 minutes after, extraction of teeth which were removed under general anesthesia. Positive blood cultures were obtained in more than 60 per cent of cases after extraction, though cultures were negative before extraction. When a local anesthetic, containing a vasoconstrictor, was substituted for general anesthesia, Burket and Burn obtained fewer positive cultures. Transient bacteremias occurred, nevertheless, in 17 per cent of cases, even despite capillary constriction from the epinephrine contained in the local anesthetic solution.

Discussion

Inasmuch as the recovery of bacteria from the blood stream following tooth extraction is an indication that dissemination of bacteria from the dental tissues has occurred, and since there is evidence that in a great many cases contamination of the root surface or of the pulp occurs during extraction, the significance of finding growth within the pulp or upon the surfaces

of extracted pulpless teeth must be questioned. That the entire chapter on the bacteriology of vital and pulpless teeth needs to be rewritten is further evidenced by the fact that recent studies on the bacteriology of the living, healthy pulp are at variance with those of the past.

Practically every investigator who has, at one time or another, studied the bacteriology of the vital pulp has found growth present in a greater or lesser percentage of cases. Haden [16] believed that chronic infection occurs quite commonly in the pulps of vital teeth and went so far as to say that "many believe there is a chronic infection in the pulp of every tooth in which the dentin is invaded by caries." If this were taken literally and such teeth were condemned, we should have a toothless nation, since it is estimated that more than 90 per cent of the people have carious teeth or have had carious teeth at one time. In the light of studies by Fish and MacLean, and by Okell and Elliot, it is easy to understand why bacteria were recovered from normal, healthy pulps following tooth extraction. When vital pulps were exposed and cultured in situ according to the method of Gunter and Appleton,[20] whereby contamination from the gingival crevice is eliminated, no growth was obtained. This again points to the fact that in previous studies of vital teeth, bacteria were forced into the pulps during extraction, which gave an erroneous indication of the bacteriologic status of such teeth. By the same token, bacteria were forced within or upon the surfaces of extracted pulpless teeth, from the cultures of which growth was afterward recovered. Cultures made from extracted teeth do not, therefore, reflect the true bacteriologic status whether it be of vital or of pulpless teeth, unless, as shown by Fish and MacLean, the gingival tissues are first cauterized. Since pulpless teeth fell somewhat into disrepute because of bacteriologic studies made in the last 15 or 20 years, and since the findings were generally based upon bacteriologic examinations made after extraction, without adequate means having been taken to prevent contamination, past interpretations can no longer be held valid in the light of recent knowledge. We must look to recent and future investigations rather than those of the past, to determine the bacteriologic status of the pulpless tooth. *From what is already known it is expected that such investigations will be in closer agreement with correlative studies already made of pulpless teeth by clinical, roentgenologic and histologic examinations.* To hold the pulpless tooth to the bacteriologic criticism of the past would seem unjustified.

Summary

1. A pulpless tooth is not a "dead" tooth. It still continues to have a vital relationship with the surrounding tissue.

2. The more important clinical, roentgenologic, histologic and bacteriologic studies dealing with the pulpless tooth as a possible focus of infection have been reviewed and evaluated. The accumulated evidence against the pulpless tooth, even at its worst, is not so damning. Actually, growth from pulpless teeth was recovered in about 36 per cent of cases when compared

with growth recovered from vital teeth. Recovery of growth, per se, does not indicate that infection was present.

3. Recent bacteriologic studies dealing with the pulpless tooth have been presented. These studies tend to invalidate, to a great extent, the results of previous investigations, or to interpret them in a new light.

4. In view of the evidence presented, indiscriminate extraction of pulpless teeth is unwarranted.

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A CORRELATION STUDY BETWEEN RETINAL VASCULAR CHANGES, ELECTROCARDIOGRAPHIC ALTERATIONS AND RADIOLOGICAL HEART SIZE IN ESSENTIAL HYPERTENSION *

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Introduction

In essential chronic hypertension the relative simplicity of diagnosis stands in striking contrast to the more difficult problem of prognosis. It is well known that the ultimate fate of individuals exhibiting this condition is determined by the cardiovascular diseases consequent to the hypertension, the most important of which are the cardiac hypertrophy and the arterial or arteriolar sclerosis. These changes are of particular significance when the arterioles of the brain, kidneys, myocardium and retina are involved. It is also well known that death will usually result from myocardial failure, although cerebral hemorrhage, myocardial infarction and uremia are frequent terminal events. Occasionally dissecting hemorrhage of the aorta may occur. Apart from these generalizations the problem of prognosis has been discussed in the literature more specifically with reference to various clinical manifestations, kidney function and height of blood pressure. Of the more recent objective evidence of this disease, retinal vascular changes and electrocardiographic abnormalities have been given relatively little consideration. Furthermore it has been the practice in many studies to determine heart size by palpation and percussion instead of by the more accurate roentgenologic (orthodiagraphic) method. The studies dealing with prognosis have been determined by grouping the various criteria and recording the number of individuals in each group alive at some chosen time. Since so little attention has been paid to the possibility of utilizing the material obtained from objective experience, we have undertaken to determine some of the facts in regard to the retinal vascular changes, electrocardiographic alterations and the radiological heart size in a group of patients with essential hypertension. Special attention was given to the frequency, the type and the degree of the changes and particularly to their correlation and relative value. Although the selected material in this study is numerically inadequate for a comprehensive statistical compilation, it seems sufficient to suggest a definite trend which more study would probably establish as a fact.

* Received for publication March 7, 1939.

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Material

In order to obtain uncomplicated cases of essential hypertension those cases in which one or more of the following conditions were present were eliminated: (1) glomerulonephritis, advanced prostatism, syphilis, diabetes, thyrotoxicosis, anemia (exception: one case had a moderate degree of secondary anemia), coarctation of the aorta, cardiac infarction, valvular disease (exception: one case had an atherosclerotic mitral regurgitation); (2) (from an electrocardiographic viewpoint) QRS complex larger than 0.10 sec., auricular fibrillation, evidence of cardiac infarction, old or recent; (3) digitalis medication within the three weeks preceding the electrocardiographic study. From a series of 500 cases which were studied it was necessary to exclude 420 patients because they had one or more of the above complicating conditions. The remaining 80 cases included 38 males and 42 females; the youngest patient was 12½ years of age, the oldest 73 years of age, with 55 per cent of all the cases between 40 and 59 years of age. The selected patients had a diastolic blood pressure of at least 95 mm. Hg and a systolic pressure of at least 150 mm. Hg. All of the cases had electrocardiographic and retinal studies, but unfortunately 21 cases were too ill to have a fluoroscopic and orthodiagraphic study done, which leaves 59 cases in which an orthodiagraphic study was undertaken. The question of the duration of the hypertension has been one factor we have been unable to ascertain with accuracy.

The reports on the fundi examinations, from which our study has been made, are based on the description and grouping of Wagener.[1] It seems desirable to quote his presentation of the subject:

> As seen with the ophthalmoscope, the first alterations that take place in the arterioles of the retina are narrowing of the caliber, a change to a lighter color than normal of the entire breadth of the arteriole, and exaggeration and broadening, or accentuation, of the reflex stripe. These are regarded by some as signs of hypertension in the sense of spastic arteriolar constriction or increased arteriolar tonus and by others as the commencement of actual arteriosclerosis through thickening of the media.

(In our study these cases have been classified as preorganic or presclerotic. It is thought that the retinal arterioles have been subjected to increased pressure of insufficient duration or intensity to cause sclerosis.)

> In more advanced cases, signs of definite sclerosis appear, irregularities of the lumen of the arterioles, compression of the veins at the arterial crossing and at times visibility of the vascular walls. Irregularity of lumen is the most definite sign of sclerosis, if it is not confused with the irregularity produced by spasm. Sclerosis observed in advanced cases is visible in all branches, but in earlier stages is best seen in the smaller arteries, either in the nasal or in the secondary and tertiary branches of the temporal vessels. It is usually rather evenly distributed in grade in all vessels of approximately the same size. Severity of sclerosis can be graded from 1 to 4, largely on the basis of the number of irregularities, and the degree to which they narrow the lumen of the arterioles.

If the narrowings are just barely perceptible, the case is classified as

grade I sclerosis (figure 1). If the narrowings are more numerous and cause rather obvious encroachment on the lumen, the sclerosis is classed as grade II (figure 2). If there is marked narrowing and marked caliber

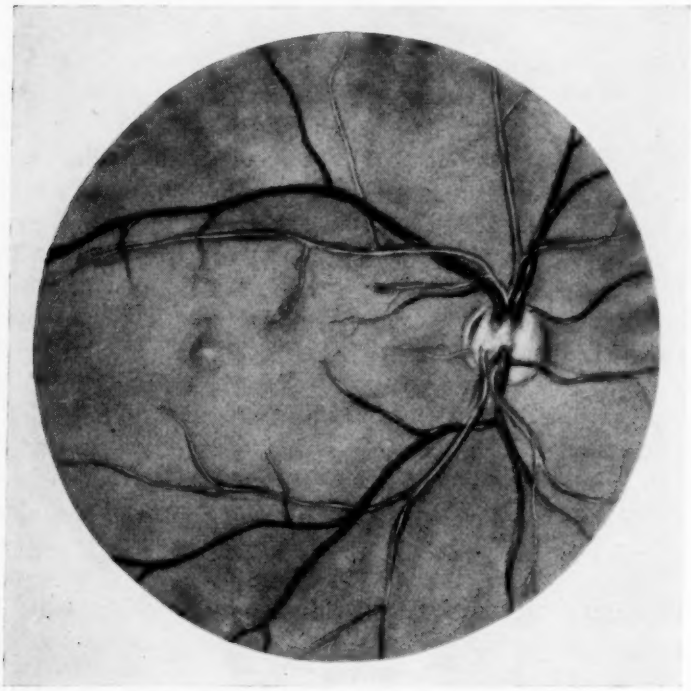

FIG. 1. Fundus picture in the presence of grade I sclerosis.

diminution, the sclerosis is classified as grade III (figure 3). If the arteriole is so reduced in caliber as to appear as a white line, this is the maximum amount of sclerosis and is said to be grade IV.

Since there is no complete agreement about the preorganic group of arteriolar constriction, we have included in our group designated as I in the tables those cases which we classified ophthalmoscopically as the preorganic group and the mildest (grade I) sclerosis.

The electrocardiographic studies were evaluated for the presence or absence of left axis deviation and aberrations of the final deflection. An alteration of the R (S) T interval level was considered significant if the deviation was equal to or greater than ½ millimeter from the base line. Since in these series we are not dealing with instances of tachycardia, the T–P level has been taken as the base line. This R (S) T interval is often depressed in Lead I, or I and II, and often elevated in Lead III. The shape has also been considered—such as straight, oblique or arched. T-wave changes were considered with reference to direction and amplitude. They may be negative or diphasic in Lead I, or I and II, and may resemble the cove plane type of T-wave observed in the course of myocardial infarction.

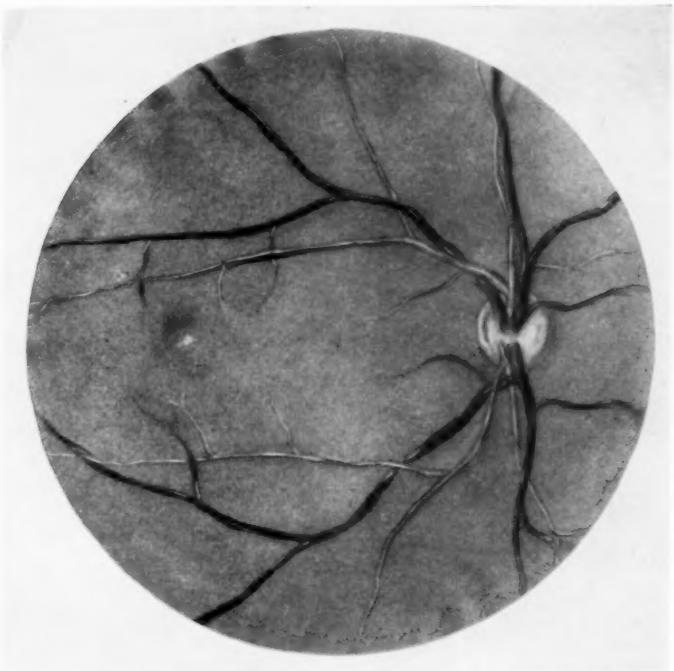

FIG. 2. Fundus picture in the presence of grade II sclerosis.

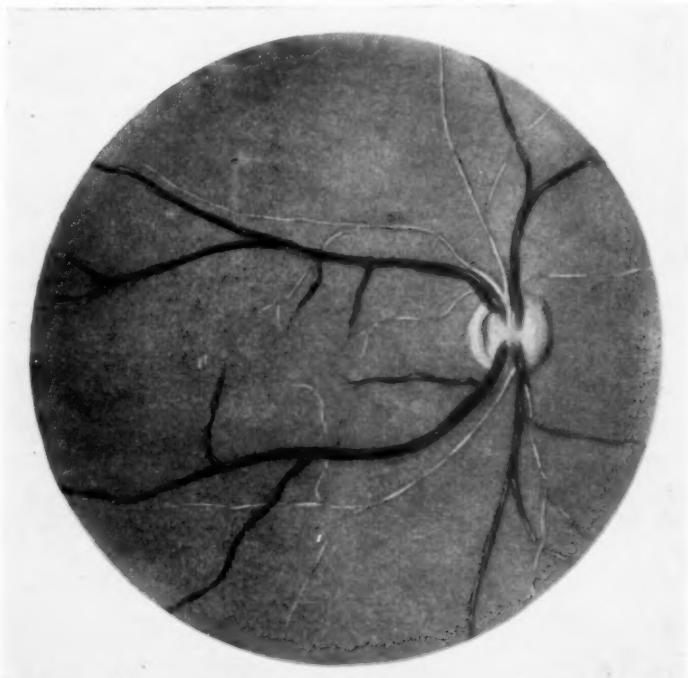

FIG. 3. Fundus picture in the presence of grade III sclerosis.

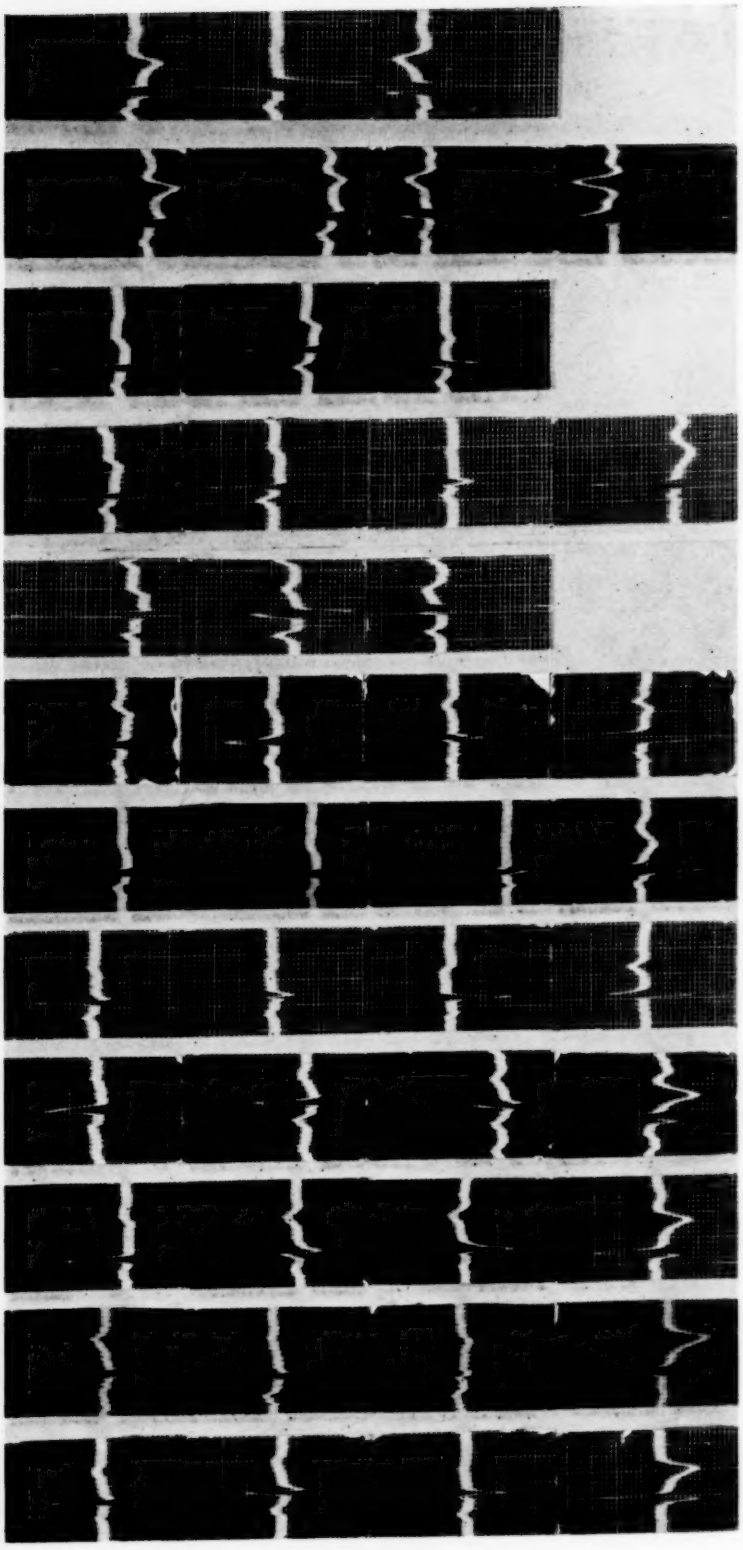

FIG. 4.

The heart size was determined by orthodiagrams. The size of the patient's chest and of his clenched fist was found to be valuable for the crude but practical subdivision into normal, slightly to moderately, and markedly enlarged.

We have found, as one might expect, a variety of combinations of final deflection changes in the electrocardiograms. Samples of these, selected at random, demonstrating different types, are illustrated in figure 4. A comparison of the three criteria, i.e., retinal vascular changes, electrocardiographic alterations and heart size, impresses one with a certain lack of correlation which will be discussed shortly.

Data

The data have been arranged in three tables. The association of electrocardiographic findings with retinal changes is shown in table 1. The association of radiologic findings, as to cardiac size, with retinal changes is shown in table 2. In table 3 the data are arranged to show the association between the electrocardiographic and the radiologic findings.

Results

(1) The fundus examination revealed retinal arteriolar changes, hypertensive type, in all of the 80 cases, with 88.8 per cent (71 cases) classified as having advanced to the stage of sclerosis, and with the remaining 11.2 per cent in the preorganic stage of the disease.

(2) The electrocardiographic study gave the following results. Final deflection changes were present in 68.8 per cent (55 of the 80 cases). Left axis deviation occurred in 75.0 per cent (62 cases). Final deflection changes were associated with left axis deviation in 57.4 per cent (46 cases), while left axis deviation occurred without associated final deflection changes in 20.0 per cent (16 cases). In 11.3 per cent (9 cases) the ECG was en-

FIG. 4. Samples of electrocardiograms from 12 cases, left to right. From above down Leads I, II, III, IV (left arm lead to electrode in left interscapular space, right arm lead to apical electrode).

(1) aged 55, no failure, but dyspnea on effort, B. P. 220–120, heart slightly enlarged. Fundi: grade I sclerosis, marked angiospastic features. (2) aged 51, no failure, B. P. 160–105, heart slightly enlarged. Fundi: grade I sclerosis. (3) aged 50, slight degree of failure, B. P. 240–110, heart moderately enlarged. Fundi: grade II sclerosis with retinitis of severe benign hypertension. (4) aged 46, no failure, B. P. 180–125, heart slightly enlarged. Fundi: marked vasospastic changes in retinal arterioles. (5) aged 50, no failure (angina pectoris), B. P. 200–140, heart normal in size. Fundi: grade I sclerosis and vasospastic changes. (6) aged 67, slight degree of left-sided failure, B. P. 220–155, heart moderately enlarged. Fundi: sclerosis grade II with retinitis of malignant hypertension. (7) aged 47, no failure, B. P. 185–95, heart moderately enlarged. Fundi: grade I sclerosis and preorganic vasospastic changes. (8) aged 32, no failure, B. P. 195–145, marked cardiac enlargement. Fundi: grade I sclerosis with vasospastic retinitis. (9) aged 51, very slight failure, B. P. 230–130, moderate degree of cardiac enlargement. Fundi: grade II sclerosis with retinitis of malignant hypertension. (10) aged 58, case with skull fracture, B. P. 235–135. Fundi: grade II sclerosis with retinitis of severe benign hypertension. (11) aged 50, no failure (asthmatic bronchitis), B. P. 180–105, heart moderately enlarged. Fundi: grade I sclerosis. (12) aged 52, angina pectoris and nocturnal dyspnea, B. P. 200–100, heart markedly enlarged. Fundi: grade I sclerosis and vasospastic changes.

tirely normal, as no final deflection changes or left axis deviation were present. Since left axis deviation may also occur, so to speak, physiologically with a certain constitutional type and in the higher age group, it cannot be considered as necessarily significant. Hence, in 31.3 per cent (25 cases) the electrocardiogram revealed no significant findings.

(3) The orthodiagraphic study of 59 cases showed absence of cardiac enlargement in 22 per cent (13 cases); a slight to moderate enlargement was present in 50.8 per cent (30 cases), and a marked degree of enlargement occurred in 27.1 per cent (16 cases).

Statistical Evaluation

Since the selected material is not large, any statistical discussion can be based only upon the trends of the data present. It is assumed that with a greater number of cases the distribution would remain relatively the same. This assumption is subject to verification by a more extensive research.

Method. As units, electrocardiographic findings were classified as either non-pathological, when there was no final deflection change (FDC), or as pathological, when there was a final deflection change. Data as to left axis deviation (LAD) are included for completeness. Retinal changes were classified as groups I, II and III arteriolosclerosis hypertensive type. Group I includes cases with narrowing of the arterioles, with increased intensity of the reflex stripe but without constriction. Cardiac enlargement was classified as none, moderate and marked. Tables 1 and 3 consist of division into six sections, and table 2 consists of division into nine sections, for a paired comparison of each clinical manifestation with the other, respectively. The material was distributed in classification boxes. Thus, for example, in table 1 the number of cases showing grade I retinal arteriolosclerosis and absent final deflection changes in the electrocardiogram have been put into one box; those showing grade I changes with final deflection changes into another box, etc. Each of the horizontal rows has been totaled, and the percentage of each class has been computed; this percentage has been plotted as a divided horizontal bar, so that regardless of the number of cases the relative lengths of the bars indicate the distribution into the three classes indicated. The sums of these horizontal bars have been treated in the same way, giving an additional horizontal bar, indicative of the average distribution of these selected cases. Each of the vertical columns has been likewise totaled, and the percentage of each class has been computed. This percentage has been plotted as a divided vertical bar, so that regardless of the number of cases the relative lengths of the bars indicate the distribution into the two classes (tables 1 and 3) and into the three classes (table 2), respectively. The sums of these vertical bars have been treated in the same way, giving an additional vertical bar, indicative of the average distribution of these selected cases.

Analysis. Table 1 (80 cases): The horizontal bars indicate an increase

of groups II and III retinal arteriosclerotic changes, hypertensive type, in cases with electrocardiographic final deflection changes, as compared to the average (lower right hand corner), and as compared to the cases with ab-

TABLE I

Relative distribution of electrocardiographic versus ophthalmoscopic findings in essential hypertension (80 cases).

E.C.G. ALTERATIONS	RETINAL CHANGES I	II	III	
F.D.C. ABSENT	16	8	1	64/32/4 %
L.A.D. ABSENT	6	3	0	
L.A.D. PRESENT	10	5	1	
F.D.C. PRESENT	24	24	7	44/44/12 %
L.A.D. PRESENT	19	23	4	
L.A.D. ABSENT	5	1	3	
AVERAGE E.C.G. ALTERATIONS	31/69 %	40/60 %	25/75 %	50/40/10 % AVERAGE RETINAL CHANGES
			12/88 %	

Abbreviations in this and the following tables: F.D.C.: final deflection changes; L.A.D.: left axis deviation. I, II, III: grades of retinal arteriolar sclerosis, hypertensive type; I includes cases with narrowing of the arterioles, with increased intensity of the reflex stripe but without constriction.

sence of final deflection changes. The vertical bars indicate a steady increase in the percentage of cases with electrocardiographic final deflection changes as the retinal examination shows an increasing grade of retinal vascular pathology. There are definitely noticeable exceptions to this positive correlation as shown in those hypertensive patients who reveal an association of final deflection changes, without left axis deviation, together with a lesser degree (group I) of retinal arteriolosclerosis (five cases, first row, second column). Conversely, one finds that an absence of final deflection changes, with left axis deviation, is compatible with a high degree (group III) of retinal changes (one case, third row, first column). Conclusion: There is a trend towards a positive correlation between retinal vascular changes and electrocardiographic alterations.

Table 2 (59 cases): The horizontal bars indicate an increase of group III, retinal arteriolosclerotic changes hypertensive type, with progressive change in heart size. The progression for group II is not regular. However, if one fuses the rows for moderate and marked cardiac enlargement, the increase for group II is quite striking, both as compared to the average (lower right hand corner) and as compared to the percentage of cases with normal heart size. The vertical bars indicate in general an increase in

cardiac enlargement together with progression in retinal vascular sclerosis. Certainly, as retinal pathologic changes increase the incidence of no cardiac enlargement is progressively reduced, and in our series normal heart size

TABLE II

Relative distribution of radiologic versus ophthalmoscopic findings in essential hypertension (59 cases).

CARDIAC ENLARGEMENT	RETINAL CHANGES I	II	III	
NONE	10	3	0	77/23/0 %
MODERATE	14	14	2	47/47/6 %
MARKED	9	5	2	56/31/13 %
AVERAGE CARDIAC ENLARGEMENT	22/51/27 %	30/43/27 %	13/64/23 %	0/50/50 %
				56/37/7 % AVERAGE RETINAL CHANGES

does not happen to coincide with group III, retinal arteriolosclerosis, hypertensive type (third row, first column). Exceptions to this positive correlation are shown in those hypertensive patients who have an association of normal radiological heart size with a higher degree (group II) of retinal arteriolosclerosis (three cases, first row, second column). The degree of correlation would presumably be greater except for the fact that 21 patients were too ill to permit a fluoroscopic study; 14 of these fell into retinal arteriolosclerosis groups II and III. Conclusion: There is a trend towards a positive correlation between cardiac enlargement and the grade of the retinal arteriolar changes.

Table 3 (59 cases): The horizontal bars indicate an increase of cardiac enlargement in cases with electrocardiographic final deflection changes, as compared to the average (lower right hand corner), and as compared to the cases with absence of final deflection changes. The vertical bars indicate a steady increase in the percentage of cases with electrocardiographic final deflection changes as the radiologic examination shows an increase in the size of the heart. Again it is possible for hypertensive patients to show an association of final deflection changes, without left axis deviation, together with a normal heart size (two cases, first row, second column). Conversely, one finds that an absence of final deflection changes, and of left

axis deviation, is compatible with a marked degree of cardiac enlargement (two cases, third row, first column). Conclusion: There is a trend towards a positive correlation between electrocardiographic changes and cardiac enlargement.

TABLE III

Relative distribution of electrocardiographic versus radiologic findings in essential hypertension (59 cases).

E.C.G. ALTERATIONS	CARDIAC ENLARGEMENT NONE	MODERATE	MARKED	
F.D.C. ABSENT	6	11	3	30/55/15 %
L.A.D. ABSENT	5	6	2	
L.A.D. PRESENT	1	5	1	
F.D.C. PRESENT	7	19	13	18/49/33 %
L.A.D. PRESENT	5	16	11	
L.A.D. ABSENT	2	3	2	
AVERAGE E.C.G. ALTERATIONS	34/66 %	46/54 %	37/63 %	18/82 % — 22/51/27 % AVERAGE CARDIAC ENLARGEMENT

DISCUSSION

An attempt will be made to discuss the three criteria and their incomplete correlation by presenting some essential data and giving those references which will be of interest to the student of these problems.

Vascular Changes in General. In any discussion of hypertension it is necessary for one to consider the pathological changes in the blood vessels. In this regard some significant facts are revealed by a perusal of the literature and from personal observations. Arteriolosclerosis is found in association with hypertension, particularly in the kidneys. However, this is merely an aggravation of a process which is present already in non-hypertensive individuals. This process is irregularly distributed in the body in general and may be segmental in arrangement within a vessel.[2, 3, 4, 5, 6, 7] In the heart these lesions are often but moderate in intensity or insignificant altogether and have neither a relation to the degree of the atherosclerosis in the main branches of the coronary arteries nor to the degree of fibrotic scarring in the heart muscle.[4, 8, 9, 10, 11] Such discrepancies in the distribution of the arteriolosclerotic process have been pointed out for the retinal vessels likewise, by comparing the findings in the central retinal artery with those in the retinal arterioles,[12, 13] or the retinal arterioles among themselves.[14] That there is no strict parallelism between changes in the retinal vascular tree and the arteriosclerosis of the larger peripheral vessels,[15, 16, 17, 18] or of the larger basal cerebral vessels[19, 20] has been demonstrated.

Retinal Vascular Changes. Classical ophthalmoscopic descriptions have been given in the last century.[15, 21, 22] The significance of arteriolar disease as a basis of the so-called albuminuric retinitis has likewise been recognized,[23,24] while later on the ophthalmoscopic characteristics of the arteriosclerotic [25] and of the ischemic, angiospastic [26, 27] retinitis have been described. For the details, we refer to some of the more recent excellent publications.[28, 29, 1, 30, 31]

Associated with vascular sclerotic changes there may occur in the retinal tissues hemorrhages, edema, and finally, in association with spastic changes in the vessels, ischemia and focal necrosis. The occurrence of various combinations of such lesions has been referred to as retinitis, although the processes are quite different from those usually designated as inflammation. Retinitis of hypertension may occur in the preorganic phase of the disease when the severity of the lesion progresses from increased arteriolar tonus to actual spasm of the vessel. Retinitis seldom occurs with grade I sclerosis, occasionally with a grade II, usually with a grade III, and almost invariably at some time in the course of a grade IV sclerosis. The presence of a retinitis adds a definite element of gravity to the prognostic picture.

Systemic hypertension may diminish or even disappear, particularly so in the course of cardiac failure. This fall is usually more marked for the systolic than for the diastolic pressure. Retinal arteriosclerosis, however, persists and is then an important diagnostic sign, indicating that the patient had previously had hypertension.[18, 32]

It is thought that the degree of retinal arteriolosclerosis depends upon the degree and the duration of the hypertension. Although it is true that an elevation of the peripheral blood pressure, as determined in the brachial artery, is accompanied by an elevation in the pressure of the central retinal artery at the level of the disc, as determined by Baillart's dynamometer (tonoscopy), yet it has been shown that between them there exists no close parallelism. The principle of tonoscopy consists in steadily increasing outside pressure on the bulb. At a certain level of pressure the motionless central artery shows a tremor, and this indicates the moment when the diastolic pressure is equalized. The artery then is seen to empty and fill itself rhythmically, and finally the pulse just before the complete collapse indicates the systolic pressure. The diastolic retinal pressure can always be determined while the measurement of the systolic pressure has its limit at about 150 mm. Hg. Several investigators have published data revealing a rather wide range in the ratio of the diastolic retinal to the diastolic brachial pressure.[33, 34, 35, 36] In a series of 20 cases the ratio varied from 0.30 to 0.96,[33] and from 0.48 to 0.84 in another study comprising 31 cases.[35] * If it is assumed that the tension in the retinal arterioles is an important factor in the development of arteriolosclerosis, it is of great significance that there is not necessarily a close parallelism between peripheral and retinal blood pressure.

* We have determined this ratio for those cases in which the diastolic pressure was 95 mm. Hg or more.

This perhaps might explain why we observe, though rarely enough, the absence of arteriolosclerotic changes in the eyes of patients who are known to have a typical essential hypertension of the non-intermittent type.

Figures pertaining to the frequency of retinal arteriolar changes in the presence of essential hypertension vary considerably.[18, 37, 38, 39, 8, 40, 41, 42, 43, 44, 45, 46] A detailed study of these reports reveals that one cause for the difference in frequency of pathological changes is due to differences in the criteria used. It seems quite likely that early changes have been overlooked and hence a relatively high percentage of normal eyegrounds has been reported. The study of the retinal arterioles demands inspection from the disc to the extremes of the arteriolar tree through a dilated pupil. Another reason for varying statements is the fact that cases with increased systolic but normal diastolic blood pressure (or even without statements as to the latter) were included in some such studies. In two very careful investigations[39, 41] the frequency of an abnormal fundus picture was found to be as high as 96 per cent and 93 per cent respectively.

Electrocardiographic Changes. Left axis deviation, increased amplitude of the initial deflection, and abnormalities of the final deflection are often, though not regularly, found in association with hypertensive heart disease.[47, 48, 49, 50, 44, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60] Final deflection changes may well be sequelae to bundle branch block, myocardial infarction, or digitalis medication, and in some of the publications, these factors have not always received the attention which they warrant. It is not entirely clear at the present time what the rôle is of the hypertrophy, dilatation, or myocardial damage, in affecting the metabolic activity of the myocardium to produce these final deflection changes. An outlasting of the excitation rather than a delay, for the left ventricle, has been suggested.[61] The electrocardiographic pattern of left axis deviation, with final deflection changes in Lead I, or Leads I and II, has been correlated with the clinical picture,[49, 58] or with mortality rate,[55, 53, 59] or with both.[56] Also, T-wave negativity has been considered exclusively.[50] The general trend has been to ascribe to these findings a serious prognostic significance. Such a general statement is not justified in our experience. The finding indicates an advanced degree of left ventricular hypertrophy with strain but it does not seem sufficient to warrant a diagnosis of severe myocardial damage. Cases have been reported in which the aforementioned electrocardiographic pattern has been observed, and later a careful postmortem examination revealed no macroscopic evidence of coronary artery sclerosis.[52, 60]

Heart Size. The radiological evaluation of heart size gives more reliable results than those obtained by means of percussion and palpation, and that this holds particularly true for the obese and emphysematous needs no further discussion. A considerable degree of hypertrophy is compatible with a normally sized cardiac silhouette. Experience shows that heart size is not more than a fair criterion as to effort capacity and expectation of life, and that this criterion is of greater value in valvular disease of rheumatic

etiology than in the group of hearts with coronary artery disease.[62] For a complete evaluation of the prognostic significance of heart size it is necessary to know if congestive failure exists or has existed with particular reference to pulmonary congestion.

Whereas all fundi revealed at least some degree of vascular change, we find that 11.3 per cent of all cases had a perfectly normal electrocardiogram; if we exclude left axis deviation as evidence of abnormality, 31.3 per cent had a non-significant electrocardiogram. Furthermore 22 per cent showed a normal radiological heart size. The ophthalmoscopic examination, therefore, gave the highest incidence of positive findings in these carefully selected cases.

The incomplete correlation is in part explainable by the fact that no attempt was made in this study to arrange the data on the basis of the duration of the disease and the severity of the hypertension. Obviously, certain cases lack the elements of intensity or duration of their condition to bring about evidence of the disease in the electrocardiogram or roentgenogram.

The correlation between each of these criteria has not been demonstrated to be of high statistical significance. The relatively small number of cases has not permitted the computation of the coefficient of correlation.

Prognostication can be better made when follow-up studies of the three criteria are available after the elapse of several years. In view of the fact that all of the three criteria occur in varying degrees and proportions in the different cases it seems desirable for one to have an evaluation of each of these three criteria in order to attempt a careful evaluation of a given case.

Summary

Eighty carefully selected cases of essential hypertension were studied from the point of view of retinal vascular changes and electrocardiographic alterations, and 59 of them as to radiological heart size, and a correlation between these criteria was carried out.

Retinal vascular changes were noted in all of the selected cases, with 88.8 per cent graded as sclerosis, hypertensive type. The electrocardiogram revealed final deflection changes in 68.8 per cent. A slight to moderate enlargement of the heart was noted in 50.8 per cent, and a marked degree in 27.1 per cent.

There is a trend towards a positive correlation between electrocardiographic alterations and the grade of the retinal arteriolar changes, between cardiac enlargement and the grade of the retinal arteriolar changes, and between electrocardiographic alterations and the degree of cardiac enlargement. This correlation was not demonstrated to be of high statistical significance.

Some of the possible causes for this incomplete correlation are discussed, among which the irregular distribution of the vascular processes and the lack of strict parallelism between the systemic and central retinal artery blood pressure are stressed.

Inasmuch as there is an inadequate correlation between the three criteria in question, it seems desirable to have, in a given case of essential hypertension, an evaluation of the eyeground, electrocardiogram and heart size, in addition to the more routine studies, when one attempts the difficult task of making a practical prognosis for a patient who has this disease.

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HYPOGLYCEMIA FOLLOWING ENCEPHALITIS *

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THE recognition of hypoglycemia as the causative factor in the production of a fairly definite group of symptoms has commanded considerable attention in recent years. Both from experimental and clinical observations it has been associated with a wide distribution of pathological lesions. These are tabulated below.

Causes of hypoglycemia

I. New-born infants.
   A. Starvation;
   B. Diabetic mother.
II. Pituitary.
   A. Experimental ablation (uncontrolled insulin action);
   B. Deficient anterior secretion (increased insulin action);
   C. Pituitary pancreatropic substance;
   D. Simmonds' disease;
   E. Basophile adenoma;
   F. Adiposogenital dystrophy.
III. Thyroid.
   A. Experimental ablation;
   B. Myxedema;
   C. Cretinism.
IV. Adrenal.
   A. Experimental ablation;
   B. Addison's disease.
V. Liver.
   A. Experimental ablation;
   B. Hepatic destruction—carcinoma, hepatitis, cirrhosis, eclampsia, yellow atrophy, hepatoxins.
VI. Pancreas.
   A. Islet hyperplasia;
   B. Adenoma;
   C. Adeno-carcinoma.
VII. Spontaneous hypoglycemia. Spontaneous hyperinsulinism, cause unknown, comprises the majority of these cases.

At the present we are concerned only with group VII—spontaneous hypoglycemia. It is true that many cases that have been included in this group may have been due to one of the other causes, particularly lesions of the pancreas, which were not recognizable during life. It is also possible that

* Received for publication July 22, 1938.

one or more of the cases to be reported below may also be due to a definite anatomical lesion which up to the present has not been detectable.

Spontaneous hypoglycemia must result from some derangement of the equilibrium of carbohydrate metabolism. It is well known that this may occur from a variety of causes which cannot always be demonstrated upon an anatomical basis. The experiments of Claude Bernard demonstrating that puncture of the hypothalamic area would produce hyperglycemia are well known and have been amply corroborated by pathological lesions in this area. The relation of cerebral lesions to hypoglycemia has not, however, as yet received the attention that it may in future warrant.

Following are the case reports of three patients all of whom suffered from hypoglycemia, the clinical pattern of which followed shortly after what was presumed to be an attack of influenza, but in time these patients developed also a Parkinsonian syndrome of varying severity.

Case 1. A. R. C., a woman 24 years old, had had good health until February 2, 1931. For eight days she suffered from acute influenza and on February 27 had diplopia and headache.

On March 4, 11:30 a.m., there was sudden onset of sweating, trembling, syncope and loss of consciousness which lasted about an hour, during which convulsive movements were noted. On recovery from this she was very hungry and craved sweet biscuits. This was followed by a period of fatigue and lethargy. A similar attack with no loss of consciousness occurred at 5 p.m. and was relieved by tea and cake. These episodes continued intermittently, usually in late morning or afternoon, with loss of consciousness about every third one. They had been considered grand mal in character, but in late April tremors of the fingers when at rest were noticed by her family and during the next six months the classical features of Parkinsonism developed.

In October, I saw one of these attacks for the first time. She was unconscious, sweating and had generalized twitchings. Her pupils were unequal, the skeletal muscles rigid with indeterminate reflexes. The Babinski response was positive on one side. The blood pressure was low. Rapid recovery followed the giving of 25 c.c. of 10 per cent glucose intravenously. A later estimation of the blood sugar was 35 mg. per cent. The blood sugar curves of October 17 and 26 are illustrated in chart 1. On October 26 the basal metabolic rate was minus 4—plus 2. The plasma potassium was 19.8 mg., calcium 10.1 mg., non-protein nitrogen 28 mg. per cent. The skull roentgenogram, the fundi and the gastric acidity were normal. Systolic blood pressure 125, diastolic 85.

It was found that the ingestion of small amounts of carbohydrate at short intervals gave partial relief from attacks. Stramonium controlled the Parkinsonism to some extent but had no effect on the convulsions without proper diet. A nasal spray of epinephrin appeared to have some effect on the latter. In November it was decided to operate in the hope of finding a pancreatic adenoma. The pancreas appeared normal and about one-half of it was removed. This was followed by a slight temporary improvement. The blood sugar curves of November 10 and December 19 are given in chart 1.

During November and December, 1931, and January, 1932, minor attacks occurred which were controlled with glucose and epinephrin. Frequent small meals, high in fat, and sedatives constituted the routine treatment. On January 21, about 5 p.m., when the patient was unattended she apparently had a severe attack. Her afternoon tea

served at 4:55 was poured but remained untouched. It was her desire to be left alone at meals on account of her Parkinsonian disability. At 6:30 the maid found her unconscious. When help arrived she was dead. A partial autopsy consisting of the pancreas, spleen, liver, adrenals, thyroid and brain was obtained. All organs were essentially normal but the brain, which revealed the typical findings associated with postencephalitic paralysis agitans.

Case 2. This patient, a man, had a severe attack of influenza on December 23, 1932, which was followed by a slow convalescence. About the middle of January he had an attack characterized by a feeling of fullness in the head, violent trembling, profuse sweating and weakness in the legs. He was first seen by me on November 7, 1934. It was noticed that the right palpebral fissure was larger than the left, the right pupil twice the diameter of the left, there was tremor of the arms and legs and the hands were cold, clammy and cyanosed. Insomnia was most troublesome. His friends found that his facial expression had altered, having become mask-like and dour; and

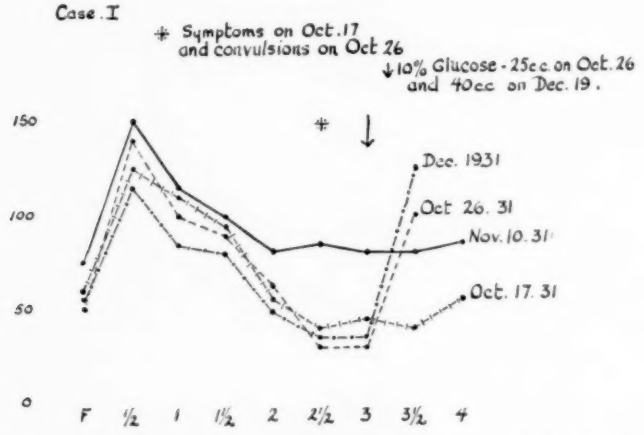

CHART 1. Four blood sugar curves of Case 1. The curves of October 14 and 26 were before operation, that of November 10 a week post-operative, and that of December seven weeks post-operative—practically identical with the pre-operative curves.

they claimed that his personality had changed, that he was irritable and secretive, had lost business ability and had decreased power of concentration. Sodium pentobarbital controlled the frequent attacks which occurred in the late morning, late afternoon and at night. Intravenous administration of glucose, 0.2 mg. per kilo of body weight, did not produce hypoglycemia. Attacks were relieved by sugar by mouth or by 0.75 c.c. of adrenalin.

The basal metabolic rate was + 13. Examination of the urine, the blood count and chemistry, the spinal fluid and a skull roentgenogram revealed nothing abnormal. The blood sugar curve is shown in chart 2.

During 1935 the attacks continued, particularly towards noon. Reduction in the carbohydrates of his breakfast gave some relief, but increasing amounts of sodium pentobarbital and alcohol were taken. In December he had an unusual blood sugar curve (charts 2 and 3). He was given 4 c.c. of ergoklonin which produced a rapid fall. On January 1, 1936 he was given 4 c.c. of ergoklonin every six hours for four doses. The blood sugar curves were flat and low. This regimen was continued for some months and the attacks became fewer. During 1937 the attacks recurred at long intervals and were mild. The patient continued to take pentobarbital and alcohol.

The blood sugar curves are shown in charts 4 and 5. In November when attacks had been absent for six months he entered the hospital where the pentobarbital and alcohol habits were successfully treated. Until March 1940 there have been no further attacks.

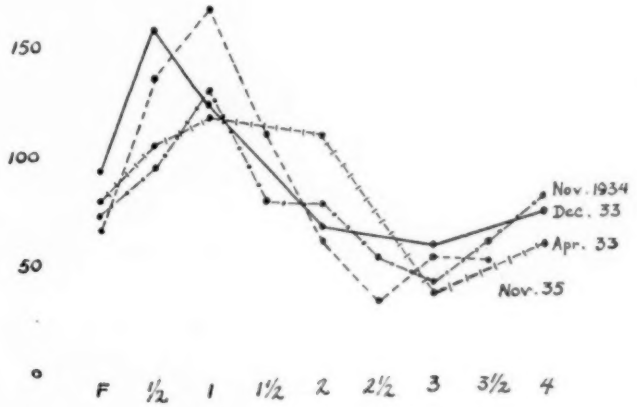

CHART 2. Blood sugar curves in Case 2, from April 1933 to November 1935, revealing a fairly consistent type of curve, with hypoglycemia between the two and half and three hours.

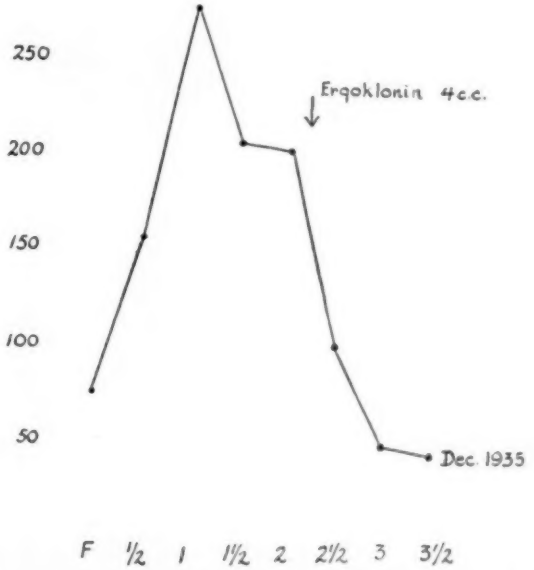

CHART 3. Blood sugar curve of Case 2 in December 1935. This was an unusual finding. Ergoklonin 4 c.c. was given which appeared to produce a sudden fall in blood sugar.

Case 3. In January 1932, a patient of Dr. Miller, Moose Jaw, Sask., had a severe attack of influenza which apparently lasted for three weeks although the patient himself does not think that he ever completely recovered. Dizzy spells preceded by occipital headaches made their appearance in May, accompanied by such weakness of the legs as to cause the patient to fall. These at first occurred about once a week,

but their frequency increased to five a week. The typical attack was always preceded by a headache which increased in severity during one and a half hours, leading to vertigo with objects rotating from right to left, ataxia and finally stupor. They were followed by weakness, trembling, sweating and irritability. Glucose or adrenalin would abort the attacks. From clerical work he turned to farming, and in the fall had his first attack of unconsciousness, which lasted one and a half hours. Another occurred a month later, both in the late afternoon.

In December he was admitted to the hospital. On physical examination he appeared normal except for tenderness in the right upper abdomen. Roentgenographic

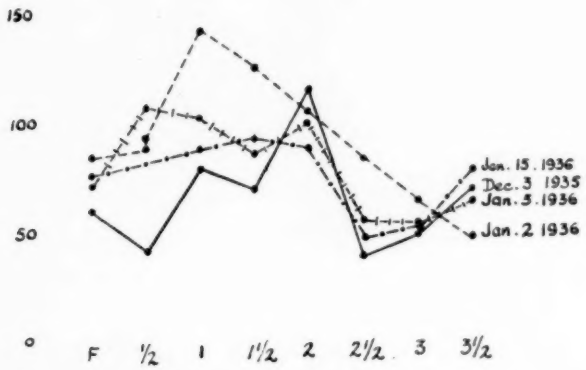

CHART 4. Blood sugar curves on Case 2 during December 1935, and January 1936, the period when the patient was receiving ergoklonin. Note the irregularity and inconsistency of the curves.

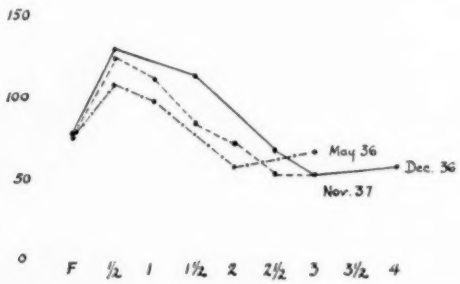

CHART 5. (Left) Blood sugar curves on Case 2 during 1936 and 1937. Note the similarity of the curves and the absence of gross hypoglycemia. The patient during this time was comparatively free of symptoms.

studies revealed a duodenal ulcer and pylorospasm. His blood pressure was systolic 114 and diastolic 72. The urine and blood examinations were negative. The basal metabolic rate was —4. The Wassermann reaction was negative and the fasting blood sugar was 42 mg. per cent. He was given a diet consisting of CHO, 100 gm., protein 60 gm., and fat 250 gm., with corn syrup and adrenalin to relieve attacks. This was followed by much improvement.

During January 1933 the high fat diet was not tolerated well; the patient refused meals and attacks became more frequent. The CHO was increased to 200 gm. and the fat reduced to 150 gm. The attacks continued but were relieved by concentrated

CHO hourly. The blood sugar curves during January and February are shown in chart 6.

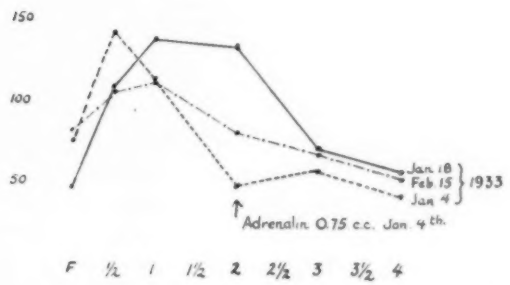

CHART 6. (Right) Blood sugar curves on Case 3 before operation.

On March 18 the possibility that a lesion of the pancreas might be present prompted abdominal exploration. No pancreatic tumor was found, but about two and a half inches of apparently normal pancreas were removed. The blood sugar curve of March 24 is shown in chart 7.

During April the attacks of dizziness returned, and on May 17 the patient had a late afternoon period of unconsciousness. A blood sugar curve of May 22 also appears in chart 7.

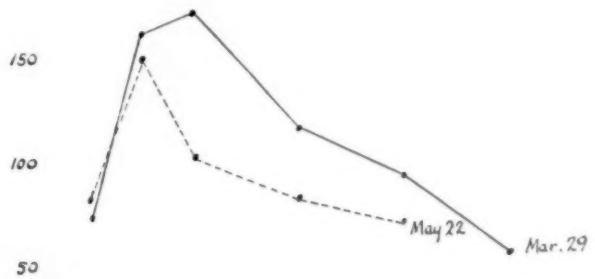

CHART 7. Blood sugar curves on Case 3 after operation. Note the temporary improvement in the curve of March 29, one week after operation, and compare with similar improvement revealed in the curve of Case 1, on November 10, chart 1.

Since 1933 there have been occasional attacks of unconsciousness. In 1936 he made an uneventful recovery following a broken arm. That fall he had hallucinations of obscure animals when he was in the dark. At present he shows absent-mindedness, inability to concentrate and irritability. He also has anorexia and abhors fats. The attacks are controlled with frequent CHO feedings.

These cases are reported in the hope that others of a similar nature may be detected. It is merely suggested that there is a connection between a possible hypothalamic lesion due to a post-influenzal encephalitis and the hypoglycemia. Certain experiments would tend to support this possibility. Miki (1932) found that hypoglycemia occurred following injury to the paraventricular nucleus in rabbits. D'Amour and Keller (1933) reported hypoglycemia in five out of 13 dogs following bilateral transverse lesions of the chiasmal end of the hypothalamus. Barris and Ingram (1935) also

produced hypoglycemia in 10 cats. The lesions were not always of constant distribution; in eight there was injury of the anterior hypothalamus, in two in the tuber region, in the posterior hypothalamus in two, and injury or atrophy of the nucleus filiformis in eight. They also noted that the hypoglycemia was often intermittent.

Clinical observations to substantiate these experimental findings are very rare. Adlersberg and Friedman (1934) reported upon the carbohydrate metabolism in post-encephalitic Parkinsonism in 21 cases. In only three did they find definite hypoglycemia following a hyperglycemia after the ingestion of 50 grams of glucose. The evidence, therefore, is still incomplete as to whether there is a true correlation between hypothalamic lesions and hypoglycemia, and further, if this should be so, whether the effect is operative through the pancreas, liver, or adrenal. To answer these questions will require more extensive experimental and clinical investigations. It seems quite likely that a spontaneous improvement may occur in these cases without extirpation of part of the pancreas.

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THE PROBLEM OF RHEUMATISM AND ARTHRITIS

REVIEW OF AMERICAN AND ENGLISH LITERATURE FOR 1938

(Sixth Rheumatism Review)*

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In Two Parts

CONTENTS

Part II

* This Sixth Rheumatism Review was prepared by the Editorial Committee (Dr. Hench, Chairman) of the American Rheumatism Association. The editorial comments express the opinion of the Editorial Committee, the authors of the Review, not that of the Association.

Part II

Chronic Arthritis: The Great Types

Clinical and Etiologic Relationships. Only a few years ago the majority of students of this subject were content to write of "chronic arthritis," making little or no attempt at a finer distinction. But such an abundance of evidence has accumulated indicating unmistakable clinical, chemical, immunologic, pathologic and radiologic differences between the several forms of "chronic arthritis," particularly the atrophic and hypertrophic forms, that few indeed are the current writers who fail to make the distinction. One physician [768] reported 150 cases of chronic arthritis which he carefully classed into atrophic, hypertrophic and mixed forms, but in his subsequent detailed analysis he ignored the classification and grouped them all together "as it appears that fundamentally they are the same disease." This is unfortunate because it makes it almost impossible to consider such a report in relationship to other current studies. It is the privilege of any physician to believe (as some authorities [763] still do) that, despite certain striking differences, atrophic and hypertrophic arthritis have close basic relationships, but nowadays when such physicians wish to command the attention of serious students of the subject, they carefully preserve the now generally accepted amenities of classification, and discuss the clinical features of each group separately. This done they are at full liberty to call attention to the supposed common attributes of the different types. The fact that so few contributors to the literature under review stressed the relationship affords evidence that the trend of rheumatology is to make the distinction between the great types more and more, rather than less, definite.

Atrophic (Rheumatoid, Proliferative, Infectious) Arthritis

Relative Incidence. Although atrophic arthritis is "the real scourge," it is responsible for less than 50 per cent of the cases classified as "rheumatism." [63, 64] There were only 1,842 cases of atrophic arthritis among 5,000 cases of "rheumatism" at the Institute of Ray Therapy, London. According to Beaumont many cases of "arthritis" in reality are due to fibrositis.

Influence of Climate, Geography and Race on Incidence. Many patients of Coste and Forestier were affected badly by sea climate, whether that of the Mediterranean, the cold windy English channel or the Atlantic Ocean. They felt worse in northern France and in the damp western French plains, better in warm dry sections away from the sea. Atmospheric dryness and low electrical potential, "which is especially low in towns," seemed more important factors than temperature. "It is not proved that polyarthritic patients feel worse in winter than in summer. Some of them bear great heat badly and have a severe attack in August," perhaps from the effects of atmospheric ionization. Hodge noted in India a juvenile form of rheumatoid arthritis which somewhat resembled acute rheumatic fever (high fever,

severe articular pain and swelling, tendency for slight relative mitral insufficiency to develop " from toxic myocarditis "), but the articular symptoms persisted unresponsive to salicylates, and true valvulitis did not develop.

Sex and Age Incidence. Of 343 patients seen by Thompson, Wyatt and Hicks 153 (45 per cent) were males, 190 (55 per cent) were females. [The usual sex incidence is about one male to two or three females affected.—Ed.] Among these same patients the disease began among both males and females at an average age of 37 years. The youngest patient was aged two, the oldest, 71 years. Although the greatest incidence is between the third and fourth decades of life, the disease may occur at any age.

Effect of Difference of Constitution on Incidence. The cases of Breuer bore no relationship to body weight or physical constitution.

General Clinical Data: Symptoms and Course of Atrophic Arthritis

The well-known British classification [119] which divided atrophic (rheumatoid) arthritis into a " primary type " of unknown etiology and a " secondary type " caused (presumably) by infection was defended with scant enthusiasm by Edgecombe and Ellman [281] to whom the clinical, pathologic, biochemical and radiologic features of both seemed very similar, if not identical. Van Dam also saw no significant radiologic differences between " infective " and " rheumatoid " arthritis. But Stone regretted the confusion of " chronic infective arthritis " with " rheumatoid arthritis." More descriptive than " rheumatoid arthritis " was Charcot's old term " progressive symmetrical polyarthritis," a disease characterized by its predilection for young women, pyrexia of low grade, anemia, loss of weight, malaise, symmetrical involvement of joints (usually hands first) and roentgenograms which reveal generalized decalcification of bone not seen in " chronic infective arthritis." On the contrary chronic infective arthritis may not affect joints symmetrically, may not begin in hands and may long affect one large joint. Although they approved the clinical separation of these two supposed types, Copeman [215] and Stone admitted that both types " demand the same therapeutic measures and respond in much the same way."

[Fewer English writers than usual supported this distinction which is rarely accepted in the United States.—Ed.]

The prodromal symptoms of " the pre-arthritic stage " of the disease were reviewed.[215] Clinical details in 343 cases of atrophic arthritis were reported by Thompson, Wyatt and Hicks, in 50 cases by Breuer, and in 165 cases (involving shoulders) by Kuhns. Blood pressures in Breuer's cases were " as one would find in a similarly sized group of persons selected at random." Thompson and his colleagues, being located at Tucson, a rheumatism resort, saw arthritic patients of the " last resorter " type; the average duration of their disease when they were seen was 6.5 years: deformities were already present in 60 per cent of the total, in 55 per cent of the females, in 45 per cent of the males.

Among 1765 patients with atrophic arthritis studied by Kuhns, shoulders were affected in only 165 (9 per cent). They were affected with equal frequency at all ages and in both sexes, but especially in (half of the) patients with atrophic (Strumpell-Marie) spondylitis. In atrophic arthritis when shoulders are affected, both are involved usually. Pathologic reactions therein are similar to those of other joints, but symptoms are greatly out of proportion to roentgenographic changes. There was rapid destruction in only three of Kuhn's cases, severe damage visible in roentgenograms in only eleven, ankylosis in six, unilateral subluxation in one. Muscle atrophy was common; tenderness, uncommon; palpable swelling, rare. "Marked swelling [of shoulder joints] is seen only in such conditions as tuberculosis or suppurative arthritis, never in chronic arthritis." [Bursitis sometimes produces marked swelling at shoulders. —Ed.] Extensive pathologic changes were commonly seen in acromioclavicular joints, but no ankylosis. Arthritis of shoulder joints tends to progress slowly, generally without the exacerbations which affect weight-bearing joints, and often almost painlessly, to a stage of marked limitation of motion unless early vigorous treatment is instituted.

Anomalies of the skin, sometimes seen in atrophic arthritis, were listed by Barber and Pringle as a cold clammy state simulating Raynaud's disease, pigmentary disturbances, psoriasis, lupus erythematosus, erythema induratum and subcutaneous nodules. The association of psoriasis with chronic arthritis will be discussed further under the heading "Psoriatic arthritis."

Atrophic Arthritis: Special Clinical Features

Effect of Jaundice. When patients with atrophic arthritis (or with primary fibrositis) become definitely jaundiced a notable event usually occurs: their rheumatic symptoms are rapidly, markedly and generally completely alleviated for some weeks or months. This phenomenon, casually mentioned by Still (1897) and by Wishart (1903), was discussed in detail by Hench (1933). Hench [430, 432] has reported further observations on the phenomenon as it appeared in 19 more cases of atrophic arthritis and in nine more cases of primary fibrositis. Observations also were made of four patients with atrophic arthritis and of nine patients with other types of articular and neuritic complaints who were *not* relieved of symptoms coincident with jaundice.

Symptomatic remissions lasting from 5 to 82 (average 18.5) weeks occurred in the 19 new cases of atrophic arthritis (average duration 5.5 years) in which intrahepatic or obstructive jaundice lasted an average of 9 weeks. Remissions of from 4 to 104 weeks occurred in nine cases of primary fibrositis in which the jaundice lasted an average of 5.6 weeks. (Two patients with lumbosacral and sciatic pain and one with secondary hypertrophic arthritis of hips had jaundice and symptomatic remissions; both jaundice and remissions lasted an average of five weeks.) The degree of relief obtained was complete in 12 (63 per cent) of the 19 cases of atrophic arthritis and in all of the nine cases of fibrositis; it was notable but incomplete in seven (37 per cent) of the arthritic cases. "Relief" implied notable or complete amelioration of symptoms of active disease. Articular pain, active articular swelling, muscular stiffness, soreness and fatigue were reduced markedly or disappeared. Residual articular thickening and stiffness from deformity were unaffected.

Jaundice developed in four cases more than once: mild jaundice did not produce remissions in rheumatic symptoms, but when jaundice was more intense the phe-

nomenon of relief was repeated with each attack of jaundice. No cumulative effect was noted; subsequent remissions were not necessarily longer than the first. When the phenomenon was invoked, it generally appeared promptly, often dramatically, usually within the first two or three days of visible jaundice, but occasionally even before jaundice was visible. The phenomenon was usually obvious to those affected and evoked such remarks as "When the jaundice came in the front door the rheumatism went out the back door." Spontaneous jaundice induced a remission, not a cure. The duration of remissions bore a general, but not a specific, relation to the intensity and duration of the jaundice. Remissions lasted from three weeks to several months; they averaged roughly from two to three times the average length of jaundice. Subsequently, rheumatic symptoms returned "as before" in 48 per cent of cases, less intensely in the rest.

In general the phenomenon was dependent more on the quantity than on the quality or "type" of jaundice. It was invoked by catarrhal, infectious, or spontaneous intrahepatic jaundice, by "cinchophen jaundice" and by obstructive jaundice from stones or malignancy. A mild jaundice was generally ineffective, the "zone of therapeutic effectiveness" seemed to begin at, and continue above, a level of about 8 mg. of bilirubin per 100 c.c. of serum. In four cases of atrophic arthritis with mild jaundice (serum bilirubin below 4 or 5 mg. per cent) relief was not noted. Intercurrent jaundice of several types and degrees did not alleviate symptoms of nine patients with other painful conditions (acute gouty arthritis, "toxic" or infectious arthralgia, juxta-articular malignancy, ischemic neuritis, postherpetic neuralgia. Therefore the phenomenon appears (so far) to be relatively specific for atrophic arthritis and primary fibrositis.

Conclusions of Hench were as follows: 1. Atrophic arthritis (and fibrositis) can no longer be regarded as necessarily relentless, uncontrollable diseases for which no rapid method of control should ever be expected. Although certain pathologic changes may be permanent, the pathologic physiology of these diseases is more rapidly reversible than previously supposed. 2. Regardless of the supposed validity of the infectious theory, atrophic arthritis and fibrositis can be affected profoundly by a phenomenon primarily chemical. 3. Nature possesses a highly effective method of producing dramatic remissions involving a phenomenon which is precipitated more rapidly by jaundice than by any other physiologic or therapeutic method.

This phenomenon was also noted by Thompson and Wyatt[950] in two cases.

One patient with atrophic arthritis had jaundice from neocinchophen (serum bilirubin 24 mg. per cent) which lasted 30 days, during which time "articular symptoms were entirely relieved." In another case, that of a child with severe polyarthritis, severe jaundice developed after a transfusion. Jaundice was intense (serum bilirubin 12 mg. per 100 c.c.) but lasted only five days; nevertheless "with the onset of jaundice the swelling and pain diminished, the arthritis completely disappeared and the child remained well for 16 months, after which symptoms returned with less severity."

Attempts which have been made to reproduce the phenomenon as a form of experimental therapy for atrophic arthritis will be discussed under treatment.

Hartfall, Garland, and Goldie[5] noted no ameliorating effect from the jaundice induced by gold salts. [The concentrations of serum bilirubin were not reported in these cases, but in at least 13 of the 85 cases of "gold jaundice" the

jaundice was "severe."—Ed.] But Burt [145] noted the "temporary cure" of a patient taken ill with jaundice after gold injections.

[The mechanism whereby jaundice operates to invoke this phenomenon can be determined only by noting what types and degrees of jaundice produce it and what types do not. Hence further observations on the effects on atrophic arthritis of jaundice related to chrysotherapy seem important.—Ed.]

The ameliorating effect of jaundice in two cases of sciatic pain (associated with fibrositis in one case, with pelvic malignancy in the other) was reported by Hench (1933). Lichtman, extending this observation, reported an interesting association among sciatic neuritis, hepatic disease and jaundice in five cases.

Case 1. The patient had had indigestion for many years before "sciatica" developed. After the latter had lasted six months jaundice developed spontaneously. [The concentration of serum bilirubin was not given.] "With the onset of jaundice" the pain in the left lower extremity became milder but did not disappear. At death, subacute liver atrophy was found.

Case 2. The patient had had salvarsan for syphilis and five years later severe sciatica. Spontaneous "catarrhal jaundice" developed three weeks after the sciatica. "The sciatic pain subsided with the onset of the jaundice," and had not recurred four years later.

Case 3. A patient at the age of 26 years had paratyphoid fever, and a year later severe sciatica. Enlargement of spleen and liver were noted respectively two and four years after the fever. When he was aged 43 years sciatica returned and continued intermittently for two years. Then nausea, fever and jaundice developed, and "the sciatic pain subsided." When the jaundice subsided the sciatic pain recurred.

Case 4. A patient had severe sciatic pain unrelieved by various measures. Twelve weeks later 5 grains of cinchophen were taken but were not regarded as responsible for the anorexia, epigastric distress and jaundice which developed one week later. "The sciatic pain definitely subsided with the onset of jaundice." At death subacute liver atrophy and pancreatitis were noted.

Case 5. This patient had sciatica with "excruciating pain." The icterus index of blood was 15; the bilirubin content was 0.6 mg. ("slightly elevated"). Two weeks later they were 8 and 0.3 mg. respectively ("normal"). "The decrease in the latent jaundice occurred simultaneously with the subsidence of pain."

Commenting on these cases Lichtman stated that the relief from pain attributable to the analgesic effect of jaundice "was greater than could be expected from confinement to bed alone." He therefore tested the analgesic effect of bile salts by introducing them into the spinal canal of cats: no analgesia was produced. He suggested that endogenous toxic substances, responsible for the peripheral sciatic neuritis, may also be responsible for hepatic injury.

[The observations of Hench and Lichtman on the ameliorating effect of jaundice in two such dissimilar conditions as atrophic arthritis and sciatica suggest that the effect is nonspecific in character.—Ed.]

Influence of Pregnancy. During the last century many physicians have believed that chronic arthritis is related etiologically to defective catamenia, other uterine disorders, the menopause, too rapid childbearing or prolonged

lactation, and that pregnancy is dangerous for women with arthritis because disease of the joints is likely to flare up after parturition.[431] The latter point is illustrated in the case of De Sa.

Eight months after completing her first pregnancy a woman developed severe progressive "arthritis deformans" of hands and feet, unrelieved by therapy. Three years after birth of her first child she conceived again: "During this pregnancy she suffered now and again from pains in fingers and toes." A month after the second confinement an acute exacerbation of polyarthritis developed which eventually necessitated tenotomies and amputation of deformed toes so that she could walk. Even so she was crippled badly. The patient was later (time unstated) seen by De Sa in the second month of her third pregnancy. Suspecting that some latent pelvic or other focus of infection was somehow activated by pregnancy and fearful of another postpartum exacerbation, De Sa terminated the pregnancy by hysterectomy.

[It should be noted that both the primary arthritic attack and the subsequent exacerbation came respectively 8 months and 1 month *after* parturition, not during pregnancy.—Ed.]

Hench studied the effect of 37 pregnancies on 22 women with chronic articular disease and concluded that, regardless of the aftermath, pregnancy, like jaundice, initiates a physiologic state which is decidedly beneficial (at least temporarily) to patients with certain articular diseases, notably atrophic arthritis.

Fifteen of the patients had atrophic arthritis, one had atrophic arthritis with recurring symptomatic hydrarthrosis; one had true (idiopathic) intermittent hydrarthrosis independent of later atrophic arthritis in other joints; one had localized lumbar arthritis, presumably infectious; two had psoriatic arthritis and two had periarticular fibrositis. Twenty of the 22 patients obtained marked, generally complete relief of articular symptoms during pregnancy and for variable periods thereafter. These 20 patients had 34 pregnancies, in 33 of which the phenomenon of relief appeared; the phenomenon did not appear in a case of early tubal pregnancy. Thirteen patients experienced the phenomenon in one pregnancy; three noted it with each of two pregnancies, two noted it three times, one noted it four times, and one noted it in each of her four intra-uterine, but not in her (fifth) tubal pregnancy. Articular relief began generally (in 16 instances) about the fourth week of pregnancy, occasionally not until the sixth week or the fifth month of pregnancy. Pain, swelling and stiffness were relieved markedly (during 13 pregnancies) or completely (during 19 pregnancies). The relief was obvious to the patients: one stated, "There's no relief like pregnancy"; another decided she "ought to keep pregnant all the time." Three patients deliberately became pregnant to enjoy the relief which one had experienced during a previous pregnancy and which two had heard of. The symptomatic remissions induced by pregnancy generally ended about four to eight weeks after parturition, occasionally considerably later. The average duration of relief was 9.4 months (shortest 5, longest 30 months). Return of articular symptoms bore an inconstant relationship to postpartum lactation and restoration of menstruation. After parturition the disease returned "as before" in eight cases, slowly and progressively in five, precipitously in four. In one case the disease was progressively less severe after each of four pregnancies.

Two women with moderately severe atrophic arthritis were apparently unrelieved by one and two pregnancies respectively: one of these, unrelieved by two pregnancies, also had noted no articular relief during a previous attack of jaundice (of unknown intensity).

[Several casual references have previously appeared [431] concerning the beneficial effects of pregnancy on intermittent hydrarthrosis, and also on atrophic arthritis. Passing comments on the latter were made by Garrod (1890), Strangeways (1907), Pemberton (1920), Llewellyn (1927), and Murphy (1936). Perhaps the most interesting comment of all appeared recently in "Queries and Minor Notes." [785] An anonymous physician commented thus: "A woman, aged 38, with polyarticular arthritis for the past 10 or 12 years, is entirely free from symptoms during pregnancy. She had nine pregnancies with return of the trouble between the termination of each labor and the next pregnancy. There is a definite aggravation of symptoms during the menstrual period."—Ed.]

It seemed logical to Hench to believe that the agents responsible for both of these phenomena (relief from pregnancy or from jaundice) are closely related, probably identical, and if the agent is a chemical substance, it is probably neither bilirubin (which does not rise appreciably in pregnancy) nor a strictly female sex hormone (since jaundice relieved male arthritics). Such diverse substances as cholesterol (which increases in the blood during pregnancy), ergosterol (the precursor of vitamin D), some of the sex hormones, cortin, and bile acids are closely related: they all contain the phenanthrene nucleus. "If the potent common denominator of these two phenomena can be discovered, progress in treatment may be expected."

Touw and Kuipers also saw three patients whose articular symptoms were relieved markedly during pregnancy.

Case 1. A woman, aged 34 years, had had progressive "primary chronic polyarthritis" for 14 years. She had borne five children: "During her pregnancies she did not know what rheumatism was." When seen later she had markedly active polyarthritis again.

Case 2. A woman, aged 37 years, had had "primary chronic polyarthritis" for seven years, with incomplete relief under treatment by solganol. Three years after this treatment she was seen in the fifth month of pregnancy "entirely free from complaints," but articular symptoms returned within six weeks after parturition.

Case 3. A woman, aged 26 years, had progressive bilateral stiffening of hips ("secondary arthrosis deformans" from old developmental epiphysitis); pain was worse before menses. After marriage she suddenly noticed that walking and cycling had become easier and practically painless. She could not account for this until a few weeks later she understood that she was pregnant. "Throughout the pregnancy the complaints had ceased. About four weeks after confinement, however, they returned, and have not left her to date."

Because of these observations Touw and Kuipers administered progestin with apparently successful results in two of the three cases.

[Another of us, M. H. D., has also studied the relationship between pregnancy and atrophic arthritis in 20 cases. As a rule the patients were considerably relieved of their arthritis during pregnancy, especially during the third trimester. Usually the arthritis became worse after delivery. However, in some cases the arthritis was apparently worse during pregnancy. In order to explain these phenomena various factors must be considered: the change in the patient's physical activities, the psychologic effect of pregnancy on the patient, and so forth. But it seems certain that pregnancy does exert a true physiologic effect in some cases of atrophic arthritis, and it is well-known that pregnancy exerts an inhibitory effect on certain other chronic diseases, notably tuberculosis, syphilis and psoriasis. Since this is true and since one of us, P. S. H., noted the inhibitory effect of pregnancy not only in atrophic arthritis but in fibrositis and intermittent hydrarthrosis, the effect of pregnancy would

appear to be nonspecific. Its relatively nonspecific nature makes the phenomenon seem less interesting to some physicians, less "tangible" and less important as a study for research than if it were specific for atrophic arthritis. But to other physicians the fact that the phenomenon may be relatively nonspecific makes a search for its cause all the more attractive. Perhaps by studying the mechanism whereby pregnancy inhibits these diseases some therapeutic procedure of wide applicability may be discovered.—Ed.]

Effects of Starvation and Anesthesia. Occasionally one will read the casual statement that a patient with atrophic arthritis noted marked, if temporary, relief after anesthesia or some regimen involving complete starvation or semistarvation. Partial relief from the low caloric, low carbohydrate diet of Pemberton has been frequently commented on. One of us (P. S. H.) has seen a few arthritic patients who claimed to have received rapid and complete, but short-lived, relief after undergoing a few days of complete starvation at a western "Health School," and in one case he reproduced the phenomenon briefly. Thompson, Wyatt and Hicks observed remarkable reduction in the doughy swellings of atrophic arthritis after starvation, nausea, vomiting, diarrhea, and ether anesthesia. Except for the studies of Pemberton and of Pemberton and Scull [3] on low caloric regimens, these phenomena have received little or no scientific study.

[The effect of starvation (as contrasted to semistarvation) and of anesthetic agents should be examined further.—Ed.]

"Opera-Glass Hand." A rare deformity in chronic rheumatic disease is "la main en lorgnette" (Marie and Leri, 1913) or "opera-glass hand." In this condition, during severe and chronic polyarthritis absorption of phalangeal bone occurs to such an extent that telescoping of fingers results, with the appearance of transverse folds in the excess skin of the fingers, giving a paw-like appearance to the hand. The case of Marie and Leri affected a female, aged 70 years; that of Weigeldt (1929) affected a female aged 64 years. Nelson has reported another case, that of a woman, aged 31 years, who had had chronic severe polyarthritis (historically and objectively like atrophic arthritis) for 19 years.

Many joints were affected, some of the phalangeal joints were ankylosed, others were abnormally mobile because of the destruction of bone. The ulna had been dissolved so that it tapered to a long thin core. A large renal calculus and chronic purulent pyelonephritis for which partial nephrectomy was done developed. Much later, values for serum calcium, phosphorus and phosphatase were normal; "the test for rheumatoid arthritis was positive in agglutination of specific hemolytic streptococci in dilution of 1 to 1200." After death by terminal bronchopneumonia a parathyroid adenoma was discovered. Several bones were examined but were normal, as were the other glands of the body. Speculations were made as to the possible relationship of the adenoma to the bony condition.

[Gutman, Swenson and Parsons (1934) noted absorption of terminal phalanges in a case of proved hyperparathyroidism. Marked destruction and tapering of phalangeal bones as illustrated in Nelson's photographs have also been noted in cases of severe psoriatic arthritis.[4]—Ed.]

Scleromalacia Perforans with Atrophic Arthritis. Since the description of Van der Hoeve (1930), about 14 cases of scleromalacia perforans (scleritis necroticans) have been reported; 10 were associated with atrophic arthritis. Verhoeff and King have reported another case; the eye was examined microscopically.

A man, aged 52 years, had had progressive atrophic arthritis for 15 years. On the sclera of one eye five smooth waxy nodules appeared which were covered by conjunctiva, immovable, firm and tender. The eye was removed because of chronic pain unrelieved by narcotics. In the scleral abscesses the following had occurred: necrosis, a surrounding wall of epithelioid cells, penetration of the wall by pus cells with infiltration of the necrotic area, then slow formation of abscess and destructive edema.

Association with Diabetes and Insulin Resistance. The combination of atrophic arthritis and severe diabetes is unusual (Pemberton, 1935). Marble saw a woman, aged 35 years, with atrophic arthritis (for nine years) lymphadenopathy, slight hepatomegaly, and severe diabetes which was resistant to insulin and required 240 to 675 units of insulin daily. Eosinophilia (up to 33 per cent) regarded as "an allergic response provoked by the extremely large doses of insulin" was also present. The diabetes was controlled by a single morning dose of 150 units of insulin plus 220 units of protamine-zinc insulin.

The Swollen Atrophic Hand. A condition superficially resembling atrophic arthritis confined to one hand was described by Oppenheimer and will be discussed later (under "symptoms caused by narrowed intervertebral foramina").

Pathologic Characteristics of Atrophic Arthritis

The pathologic reactions were described again in detail by Fisher and by Ghormley.

Synovial Membrane. The focal collections of round cells so frequently seen in synovial membranes in atrophic arthritis are considered by Ghormley to be nonperivascular and specific for this disease, by Fisher to be mainly perivascular and nonspecific. Inge's view was that many types of synovial inflammation produce the same basic pathologic reactions: synovial hypertrophy and hyperplasia with formation of villi and redundant folds, thickening of subsynovial layers by edema, fibrous engorgement of blood vessels and scattered foci of round cell infiltration. Any of these features may predominate in a given joint but "all are usually present in every case and with remarkable similarity" in cases of atrophic arthritis, infectious synovitis, or chronic trauma, "even in cases of osteoarthritis and of synovial osteochondromatosis." According to Inge the round cell infiltration is usually perivascular.

Jordan also doubted that the reactions of "rheumatoid synovitis" were specific. The injection of xylene or turpentine into the joints of rabbits produced synovial lesions, including round cell collections "practically in-

distinguishable" from those of human atrophic arthritis. In six cases of the latter he found that synovial changes varied with the degree and duration of the inflammation, and the microscopic picture may vary greatly in different sections taken from the same region of the same joint. Reactions in a case of only 2.5 months' duration were studied: no agglomerations of cells were seen. In older cases they were present and were apparently perivascular.

[Some of us do not believe the synovial reactions in atrophic arthritis are "specific" for that disease.—Ed.]

Muscles; Bones. In some cases wasting of bone and muscles may antedate considerably any evidence of intra-articular disease.[539]

Nodules. As noted under "Rheumatic Fever" Findlay, Hawthorne, and McEwen currently regard the nodules of atrophic arthritis as identical with or "very similar" to those of rheumatic fever. But Collins and Keil described certain differences. Special note should be made of the monographic report of Keil in which he reviews in great detail the similarities and differences between the subcutaneous reactions in rheumatic fever, Still's disease, gout, atrophic arthritis, fibrositis, panniculitis, periarteritis nodosa, and syphilis. The report (120 pages, 324 references) cannot be reviewed here.

Laboratory Data in Atrophic Arthritis

Roentgenograms. The roentgenographic features were reviewed.[154] Van Dam cited Huber (1896) as the pioneer radiologic student of arthritis. The amount of time which elapses between the onset of clinical symptoms and the earliest radiologic changes is never more than one year, according to Vesin and Volicer (1932); it may be many years according to Van Dam who stated that one of the earliest signs of the disease is a transverse contracture of the palm. This can be easily recognized by the projection of the metacarpal heads in roentgenograms: "the dorsal contour of the heads of the ulnar metacarpals moves in an ulnar direction in regard to the palm; the ulnar projections can also be seen to shift towards each other." These changes were illustrated in photographs and diagrams.

Hemoglobin and Cell Counts. The hemoglobin was "below 90 per cent" in most of Breuer's cases. There was no relation between the degree of anemia and the duration of the disease.

The total number of leukocytes was usually normal in Breuer's cases, often elevated in Collins' cases. Total number of leukocytes in Kahlmeter's 211 "stationary cases" averaged 6,681, in his 73 active cases 6,674; differential counts in the two groups were surprisingly alike, the only difference being a somewhat larger number of rod-nuclear neutrophiles (6.2 per cent) in active cases than in stationary cases (4.7 per cent). The fact that the leukocyte counts remain normal whether the case is progressive or stationary and whether sedimentation rates are raised or not does not support the in-

fectious theory. In Gibson's cases [357] of atrophic arthritis (and of ankylosing spondylitis) the mean percentage of neutrophiles was significantly greater than normal, that of lymphocytes was less than normal. Arneth counts were variable, normal counts being seen in some of Gibson's worst cases of atrophic arthritis. In general there was a significant shift to the left in atrophic, and also in hypertrophic, arthritis. (In fibrositis, and ankylosing spondylitis Arneth counts were essentially normal.)

Gibson divided cases of atrophic arthritis into two ill-defined groups according to their white cell picture. The lymphoid type with neutropenia of variable degree is associated with a shift to the left; the extreme example of this type is seen in so-called Felty's syndrome, as in the cases of Collins [5] in which the white cell picture simulated agranulocytosis. These findings are consistent with infection. The second type is more difficult to explain; although the patients are anemic, emaciated and toxic, they show a polymorphonuclear preponderance with a shift to the right in Arneth counts. Toxins, if present, appear to attack lymphocytes while the polymorphonuclears grow old and relatively numerous. These findings are unlike those in any infective process. "It is difficult to see that the leukocyte picture in rheumatism taken as a whole gives evidence either for or against an infective etiology."

There was no consistent correlation between Arneth counts and sedimentation rates [201, 357]; the two tests measure different abnormalities, the former cannot be used as a satisfactory index of improvement. Single or multiple applications of any one of several forms of physical therapy produced a drop in total leukocytes, especially polymorphonuclears, but no significant change in Arneth counts (Collins).

Sedimentation Rates. Rates were elevated in only 48 per cent of Breuer's cases, a smaller percentage than usual. [This suggests that not all of his cases were of active atrophic arthritis.—Ed.] Kahlmeter discussed biologic reactions involved in sedimentation rates. Normal rates (under 10 mm., one hour) were noted in 8 per cent of his 73 cases of active arthritis, and in 11 per cent of his 211 stationary cases (Westergren method). In these two groups respectively, rates were between 11 and 20 mm. in 10 and 12 per cent, between 21 and 40 mm. in 19 and 25 per cent, between 41 and 70 mm. in 38 and 36 per cent, more than 70 mm. in 25 and 16 per cent. Rates were not altered materially by single or multiple (over 5 or 6 weeks) applications of several forms of physical therapy.[201] Sedimentation tests afford the most useful index of prognosis and results of treatment. Shackle cited Orme to the effect that in cases of atrophic arthritis with rates over 50 mm. in one hour or 85 mm. in two hours the prognosis is relatively bad, improvement being at best very slow. In some severe cases rates periodically improve in summer, become more rapid in winter.[854]

Although the Westergren method is most commonly used, there are 17 or more different technics in current use; it is often difficult to obtain comparable values when a patient is tested by different methods. Because the test is so valuable in rheumatic cases Gibson considered it essential to insure its accuracy "so that it may be a method for precise quantitative measurement and not, as at present, a more or less vague qualitative test." Comparing various methods he concluded that the best technic in-

volved (1) use of oxalated blood with minimal or no dilution, (2) use of a tube at least 3.5 mm. in diameter ("the diameter of the tube clearly influences the rate"), (3) correction for red cell volume ("there is too great a tendency to shirk the need for this correction"). But Shackle stated that the bore of the tube used did not appreciably affect the results, and Bouton condemned the correction of rates for anemia or cell volume in rheumatic cases as "pseudo accuracy." The rate is "a nonspecific biological phenomenon with only approximate values." Hynes and Whitby described methods of correcting rates for anemia by means of hematocrit readings. A simplified method for such correction was described by Hambleton and Christianson. But the latter concluded that such a correction may introduce more errors than it eliminates, especially in cases with low cell volumes. Correction is valuable only when the cell volume is above 45 per cent, especially when the rate is relatively low. In cases with normal or subnormal cell volume "correction for cell volume is in general uncalled for." According to Shackle the most important source of error is failure to ensure exact verticality of the tube: "An inclination of two degrees out of the vertical is sufficient to double the rate, and three degrees to treble it."

The superiority of the differential serum vanadate sedimentation reaction as applied by Coke [5] to rheumatic cases was stressed by Hunt and Woodhouse. The discovery of a boy whose blood contained no fibrinogen made possible a study of the rôle fibrinogen plays in erythrocyte sedimentation. The boy's blood gave almost negligible sedimentation rates after one and two hours: hence fibrinogen plays a large, perhaps the largest, part in determining sedimentation.

Blood Chemistry. Freund discussed biochemical investigations in studies on rheumatic diseases. Despite the bone atrophy of this disease, estimations of serum calcium were "monotonously normal." Values for inorganic phosphates, phosphatase, uric acid, and cholesterol were generally normal. Distinctive glucose tolerance curves were noted by Shackle: (a sharp rise to abnormal heights but a sharp return to normal, usually without delay, and generally no glycosuria), they resembled those seen in exophthalmic goiter more than those in diabetes.

Formol-Gel Test. This test, as applied by Gibson and Richardson to chronic rheumatic patients, is a quantitative variant of the formol-gel test or aldehyde reaction of kala-azar. The test measures the rate of solidification of gelation and the degree of opacity which occurs in blood plasma to which a formalin solution has been added. It is not specific for rheumatism. [The reaction is increased in any disease with an elevated globulin.—Ed.] However, considerable but incomplete correlation between results of this test and sedimentation rates was noted. The test gave positive results in only 5 per cent of rheumatic cases with normal sedimentation rates, in 54 per cent of those with moderately rapid rates, in 97 per cent of those with very rapid rates. The correlation was notable in cases of atrophic arthritis, but in gout there was a dissociation between the results of the sedimentation and the formol-gel tests. Because of the dissociation apparent in those and other cases the formol-gel test cannot be used as a substitute for sedimentation tests, but it may be a distinctive index of rheumatic activity.

Cytology and Chemistry of Synovial Fluid. Data on the cytology and chemistry of synovial fluid in five cases of atrophic arthritis were reported by Jordan: total cell counts were 4,000 to 8,400; differential cell counts revealed

61 to 76 per cent polymorphonuclears, 22 per cent lymphocytes; value for dextrose was 17 to 76 mg. per cent (lower than the blood sugar); concentration of total protein was 4.12 to 6.65 gm. per cent, of uric acid 1.7 to 4.1 mg. per cent; of phosphates 4.0 to 4.3.

Etiology and Pathogenesis of Atrophic Arthritis

Factor of Infection. Recent work emphasizing the rôle of infection was reviewed by Gibson [358] and by Hench.[433] The latter summarized all the arguments which have been made for and against the microbic theory, and also outlined the rebuttal used by the proponents and antagonists of the theory. The argument favoring the theory rests on 21 points, each of which is, for reasons given, discounted by the opponents of the theory.

1. Foci. In current literature the relationship between infected foci and atrophic arthritis was not made more clear. Although infected foci were found in 58 per cent of the 343 cases of Thompson, Wyatt and Hicks, none were found in 42 per cent. Of those with foci the following sites were considered infected: throat or pharynx in 23 per cent, sinuses in 19 per cent, gingival tissues in 13 per cent, tonsils or remnants, teeth or urinary tract in 10 per cent of each, lower part of respiratory tract in 5.7 per cent, female pelvis in 4.5 per cent, prostate in 4 per cent, gall-bladder in 1.5 per cent and colon in 1 per cent. [This adds up to 101.7 per cent. Some patients had more than one focus.—Ed.] Because injections of Paul's cutivaccine so often produced focal reactions (bleeding gums, loosening of teeth, tender roots) in radiologically normal teeth of patients with "chronic arthritis" Cmunt considered dental infection a common cause of the disease. In McCollom's 110 cases sinuses were not abnormal historically, radiographically and clinically in 63 per cent, were "positive" radiographically but "negative" historically and clinically in 26 per cent, definitely infected in 11 per cent. Coleman and Capps noted 30 cases of diverticulosis of colon; in 11 atrophic arthritis was a major complication. Except for two cases (one of prostatitis, one of cholecystitis) no other infection was found. Hemolytic streptococci were found in the colon in 9 of the 11 arthritic cases, in the throat in none. Because stools became normal and arthritic symptoms subsided under intestinal treatment the arthritis was considered related to the diverticulitis.

[The articular lesions were not described, simply diagnosed "rheumatoid arthritis." The fact that they subsided when diverticulitis improved would be sufficient for some critics to believe that the cases were *not* of ordinary rheumatoid or atrophic arthritis. Modern bacteriology also requires that hemolytic streptococci be grouped according to the Lancefield technic before any conclusions can be drawn. —Ed.]

Most cases of "chronic infective arthritis" are due to cervicitis, according to Robinson and Robinson who stated that chronic cervicitis is 15 to 20 per cent more common among arthritic, than normal, women, and may be present as a deep-seated infection even though the cervix looks normal. The

precursor of infective arthritis was said to be a "cervicitis syndrome" (malaise, vaginal discharge, low lumbar backache, fatigue). Oldershaw expressed similar views.

The changing views of one authority on arthritis were reported by Cecil and his colleague, Angevine. In 1927 Cecil and Archer noted 200 cases of "chronic infectious arthritis" (some of which might not be so diagnosed now). Infected tonsils were present in 61 per cent, infected teeth in 33 per cent, other infected foci in 15 per cent. Thus most of the patients had one or more infected foci, and many were definitely improved when foci were removed early. Hence foci of infection seemed to play a major rôle in the etiology of the disease. But today the situation is different; foci have been so energetically removed that one might exclaim, "Where are the foci of yesterday!" Of 200 consecutive new patients with "typical rheumatoid arthritis" 70 per cent had no demonstrable foci, 10 per cent had doubtful foci; only 20 per cent had definite foci (tonsils of 27, sinuses of 11, teeth of 2). Only a few patients were improved by removal of infected foci.

To evaluate the rôle of infected foci Cecil and Angevine attempted to create various infected foci in rabbits, by using a strain of hemolytic streptococci which on *intravenous* injection had produced arthritis in about 85 per cent of animals. Arthritis was produced in only 11 of 100 rabbits when other methods than the intravenous injections were used, and large doses had to be given to a most susceptible type of animal. Arthritis developed only in those animals from which streptococci were recovered shortly after injection. For these reasons Cecil and Angevine concluded: "The time has arrived for a complete revaluation of the focal infection theory. Undoubtedly there are cases of infectious arthritis which result from focal infection. However, as far as typical rheumatoid arthritis is concerned, it would appear that chronic focal infection plays a comparatively unimportant rôle." In his Billing's Lecture on "Focal infection: quarter century survey" Bierring took a less positive stand. He approved "the more conservative attitude [which] has developed with reference to hasty diagnostic conclusions and radical removal of suspected foci of infection." "It is the patient with a focal infection who requires treatment and not the focal infection alone." But he considered that clinical and bacteriologic evidence had afforded definite confirmation of the fundamental concept of focal infection and "perchance the 'Rosenow heresy' may yet become the medical guide of the future."

2. Joint cultures. These were negative by ordinary culture methods in the five cases of Jordan.

3. Agglutination tests. In 21 of Goldie's 28 cases agglutination of hemolytic streptococci at a titer of 1 in 200 occurred; in only 1 of 20 control cases was such agglutination exhibited. In 51 per cent of Levinthal's 119 cases similar agglutination tests on blood gave strongly positive results; they were weakly positive in 20 per cent, negative in 29 per cent. Similar tests made with synovial fluid rather than serum, indicated positive reactions

in 72 per cent, negative reactions in 28 per cent. But " out of 11 serum-negative cases not less than 8 showed positive reactions in the joint fluids." Apparently there are more antibodies in tissue cells than in the circulation. This led Levinthal to espouse the idea of a nonspecific bacterial allergy as the cause of the disease.

4. Precipitation tests. In Levinthal's cases this test with hemolytic streptococci almost always gave the same results as agglutination tests.

5. Antistreptolysins. These are less often present in cases of atrophic arthritis than in rheumatic fever. Goldie noted over 200 Todd units in 15 of 60 cases of arthritis, in only 1 of 50 control cases. Antistreptolysin titers above 120 units were found in 31 (78 per cent) of the 40 cases of Koerner and Poulton. This is a higher proportion than that reported by previous workers. The titer tended to fall in chronic cases.

6. Skin tests. Goldie made repeated skin tests with extracts of hemolytic streptococci in 85 cases; results of tests were positive at some time or another in 73 per cent. They were usually positive in old burnt-out cases, usually negative in severe cases of short duration; in the latter, reactions often later became positive.

Theory of Bacterial Allergy. This theory was acceptable to some [570, 937] but not to Aschoff who stated that the " allergic phase plays no part either in osteoarthritis, or in rheumatoid diseases arising from specific or non-specific infections."

Virus Theory. Virus-like bodies obtained from exudates of patients with atrophic arthritis were injected into monkeys: no lesions resembling atrophic arthritis resulted (Eagles, Evans, Keith and Fisher).

Factor of Circulatory Disturbance. Observations on nail-bed capillaries of 48 normal persons, 89 patients with atrophic, and 35 with hypertrophic arthritis were made by Pemberton and Scull. Various abnormalities of capillary flow were noted much more frequently among the arthritics (especially those with atrophic arthritis) than among the normals, and were often influenced favorably by the use of massage, heat, exercise, aspirin and coffee. The possible significance of these and other circulatory abnormalities frequently present in cases of arthritis (as described in previous Reviews) was discussed by Pemberton and Scull who again concluded that many of the symptoms of rheumatic diseases arise from disturbances of peripheral circulation and can be alleviated by correction of the latter. Schackle regarded capillary microscopy " disappointing " and of uncertain value (no details given).

Factor of Altered Metabolism. In the usual vague fashion some writers again spoke of the disease as caused chiefly by " deranged metabolism " from improper functioning of the digestive tract.[40] No new data were given to support the idea.

Factor of Vitamin Deficiency. Normal adults on a good diet excrete an average of 30 mg. of vitamin C in urine daily. The output of six patients with atrophic arthritis was " very low," an average of 15 mg. (Hare and

Williams). The vitamin C content of blood was lower in 26 typical and in 29 "less typical" cases of atrophic arthritis (range 0.09 to 0.68; average 0.23 mg. per cent) than in 120 control cases (range 0.22 to 1.45; average 0.7 mg. per cent) according to Rinehart and others.

When vitamin C was administered, the concentration in blood generally rose, sometimes very slowly, sometimes not at all. "Apparently deficiency of vitamin C may exist in atrophic arthritis in the presence of an ordinarily adequate dietary intake." Rinehart and his colleagues considered this deficiency an important factor in the etiology of the disease. The vitamin C content of blood was low (average 0.57 mg. per cent) in five "county cases" but normal (average 1.36 mg. per cent) in five "private cases" of Sherwood; therefore he considered a vitamin deficiency not the cause of the disease, but a factor which should be combated if present.

[Some of us have noted no appreciable effects from the use of large amounts of vitamin C.—Ed.]

Factor of Food Allergy. In a group of 150 cases which included cases of both atrophic and hypertrophic arthritis Pottenger noted a variety of "allergic manifestations," nasal allergy, asthma, canker sores, urticaria, migraine, and so forth, but especially "gastrointestinal symptoms from food allergy." For these and other reasons chronic arthritis was considered to be an allergic reaction to specific foods. An offending food presumably provoked gastrointestinal symptoms one to seven days after its ingestion and an increase of joint symptoms "a few days later after the disturbance in the gastrointestinal tract is established." The use of eliminative diets produced marked improvement in constitutional symptoms within five to seven days, in muscular and articular symptoms in another five to seven days.

[This report is unconvincing. No details on case reports and no clinical or laboratory evidence of improvement were given. The indiscriminate mixture of 95 cases of hypertrophic, 47 of atrophic and 8 of "mixed arthritis" confuses the issue still further.—Ed.]

Intestinal Toxicosis. Hepatic dysfunction was vaguely incriminated by some authors.[84, 335, 720, 791]

Factor of Endocrine Abnormality. No consistent thyroid abnormality was noted by Rawls, Ressa, Gruskin and Gordon: in 52 per cent of 141 cases metabolic rates were normal (— 10 to + 10 per cent), above normal in 23 per cent, below normal in 25 per cent. Rates varied with the activity of the disease. Rates may be increased in early active cases, but are reduced when the disease becomes chronic, and tend to be normal as the disease becomes less active. [Any coexistent thyroid deficiency should be corrected; some believe it may act as an important contributing factor.—Ed.] Without giving new data Cawadias supported the idea that the disease is related to ovarian deficiency.

Neurogenic Factors. Burt, Gordon and Brown examined 50 patients for nervous manifestations, especially abnormalities of the autonomic system. Acute or chronic worry or shock antedated the onset of the disease

[sometimes by 8 to 12 months, however.—Ed.] in 27 per cent of cases; in 73 per cent of this 27 per cent a sympatheticotonic reaction to the oculocardiac reflex was present. Vasoconstriction was present in 70 per cent of the 50 cases, but in some cases peripheral vasodilation and vagotonia, not sympatheticotonia, were present. The last is therefore only one factor in the composition of the pre-arthritic soil. Sweating occurred in 92 per cent; the colon was dilated slightly in only 10 cases, spastic in none. Blood pressures indicated only a mild sympatheticotonia. Oculocardiac tests indicated the presence of sympatheticotonia among 66 per cent of 50 arthritics and 40 per cent of 50 controls; vagotonia in none of the arthritics, in 16 per cent of the controls; normal tone in 34 per cent of the arthritics, in 44 per cent of the controls. But results of atropine tests to paralyze the vagus were not significantly different in the arthritics and controls. It was concluded that patients with atrophic arthritis exhibit slight but not clear-cut sympatheticotonia and no definite vagotonia; that is, they exhibit amphotonia or increased irritability of both divisions, as seen in psychoneurosis and certain other diseases. Thus "rheumatoid arthritis tends to occur in persons whose autonomic nervous system as a whole is irritable and unstable (amphotonic). Therapeutic correction of those disturbances will only reduce symptoms and not cure the disease."

The frequency with which emotional reactions could be correlated with exacerbations of atrophic arthritis and the importance of a strong religious faith or a positive philosophy of life to control the psychogenic factors of this disease were stressed by Swaim and Harris.

Conclusions on Etiology. To current students of the disease no one theory on etiology is proved satisfactorily as yet. The pathologic characteristics of the disease are of such a type that Ghormley [355] concluded their stimulus was "probably chemical rather than bacterial." Despite the implications afforded by altered sedimentation rates Kahlmeter concluded that the absence of significant alterations in total leukocyte counts or in the Arneth-Schilling blood picture is fairly strong evidence against the infectious hypothesis. "Infection if present—whether specific or not—merely plays the part of an exciting agent. This agent need not always be an infection." Edgecomb concluded that there are no constant metabolic changes in the disease and no evidence that any endocrine disturbance bears a direct causal relationship to it.

Having summed up in detail the case for and against the microbic theory Hench [433] made two conclusions, one as a clinical investigator, one as a practicing physician: "As a clinical investigator I must conclude that the cause of atrophic arthritis is still unknown and that the evidence for infection, although very impressive, is incomplete. Although the microbic theory seems attractive its weaknesses are apparent. The disease can be profoundly affected by non-microbic chemical alterations [incident to jaundice and pregnancy]. For these and other reasons, invoking the privileges of a clinical investigator I cannot and need not now decide for or against the microbic theory with any finality. As a practicing physician, however, I cannot wait until the evidence is complete. The exigencies of practice force one to express an opinion one

way or another. . . . Therefore as a practicing clinician I have committed myself, with reservations to the microbic theory." In comment thereon Edgecombe [264] stated, "With this conclusion, I think, most of us will agree" and Gibson [353] called it "a perfectly accurate summing up of the present unsatisfactory position."

Relationship between Atrophic Arthritis and Other Diseases

Rheumatic Fever. On the basis of various clinical and immunologic data some authors [371, 543, 937] saw a close connection between atrophic arthritis and rheumatic fever. Findlay,[309] however, reviewing data for and against this idea, rejected the unitarian theory. Delatour never saw a case illustrating a transition between the two diseases.

Still's Disease. This will be discussed in a later section.

Treatment of Atrophic Arthritis

General Remarks. The treatment of this disease has varied "from the local application of rattlesnake or dog oil and salicylic acid to the injection of anything from salicylates, heavy metals and dyes, down to the removal of almost every organ in the body that is not padlocked." [514] Some physicians are distressingly pessimistic about the value of treatment. Since we know as yet "practically nothing" about the disease we remain, according to Shackle "but little advanced beyond Tom Brown's farmer, whose only infallible remedy for rheumatism was 'churchyard mould.'"

Others are more optimistic: it was White's [1029] opinion that "there is no chronic disease for which so much may be done." The ones to do it are the patient himself and his family physician because arthritis begins and ends in the home even if there is an interval of luxurious care in a hospital.[450] Hence a heavy responsibility rests on the shoulders of the general practitioner, who, although he produces no statistics, has no publicity agent and keeps his records, not on paper, but often only in his head, can often accomplish a cure by supervising simple forms of treatment in the patient's own home. Patients are in danger of falling into the hands of uninterested physicians who lack the necessary knowledge, perseverance and sustained interest.[686] Such physicians too often make but one therapeutic gesture (salicylates or tonsillectomy) and then abandon the case as hopeless. Or the patient may suffer at the hands of a so-called specialist who is "hipped" on his "method" which may utilize some one "specific." "Specifics" are usually of little value: an occasional brilliant result often is followed by many bitter disappointments. No patient should be treated merely as one of a "series of cases"; even mimeographed dietary directions should be discarded. Every patient should be treated as an individual problem and by a composite program, not by one favored remedy. "It is rarely necessary to inject several cubic centimeters of an expensive preparation into the buttocks to satisfy the patient's desire to have something done" (Myers). The disease should be considered a branch of internal medicine rather than of orthopedics.[422]

Management of Foci. The conservative removal of obviously infected foci was recommended again to improve the patient's general health. Very occasionally a "remarkable" [952] or "brilliant" [918] result is noted, but patients should be warned that such results are rare, and miraculous cures are not to be expected.[422, 686] Nevertheless some noted good results "too often to be coincidental." [952] A conservatively radical dental policy was currently advised.[514, 531, 717, 851] In the early stage of the disease Selig advocated the removal of all dental infection, including the removal of pulpless teeth or roots which give radiographic evidence of infection (but not those which do not). Others advised removal of all dead teeth and roots; in this disease all, not just some, pulpless teeth should be removed (O'Brien). But one should not expect a cure thereby. Improvement in arthritis was noted by McCollom in only 28 per cent of 46 cases in which tonsillectomy was done, in 30 per cent of 40 cases in which it was not done. Articular improvement was noted in 31 per cent of 29 cases in which infected sinuses were treated, in 23 per cent of 69 cases in which sinusitis was not present. In 6 of 12 cases of purulent sinusitis treatment of the sinusitis was followed by articular improvement. In general McCollom was disappointed in these results. Barwell considered tonsillectomy superior to diathermy coagulation: the latter method is at times useful but, contrary to the general notion, it is often difficult. According to Robinson most cases are due to cervicitis and in general the medical and surgical treatments used for it fail to remove the deep-seated infection. Robinson and Oldershaw recommended intrapelvic and intracervical diathermy, chief value of which is prophylactic. "The prevention of chronic infective [atrophic] arthritis in women lies largely in the hands of the obstetricians." At the hands of Robinson and Robinson such treatment produced marked improvement within five to nine months in cases of "infective arthritis" of less than 18 months' duration, but little or no improvement in cases of "rheumatoid arthritis."

["Improvement within five to nine months" is not very striking; such slow improvement might well be coincidental.—Ed.]

Cecil and Angevine were not impressed with results from removal of infected foci. Tonsils were removed in 20 cases: in only seven was the disease benefited; in two it became worse and in 11 it was unchanged. Sinuses were treated in five cases and teeth removed in three without benefit. In many of these cases foci previously had been treated or removed: tonsils in 92 cases with no improvement in 86, exacerbations in two; teeth in 52 cases with no benefit in 47, exacerbations in three; sinuses in 12 cases with no benefit in 10, exacerbations in two. In view of these results the internist, not the "focal specialist," should decide what focus, if any, should be removed, and his attitude should be conservative.

[With this last remark we agree.—Ed.]

Vaccines, Antigens, Filtrates. The year's data on vaccines were meager. Of 50 patients to whom Breuer gave intracutaneous injections of autogenous

vaccines, presumably of hemolytic streptococci, 45 noted some degree of improvement; sometimes the amounts of the vaccine which gave relief were "so small as to appear ridiculous." Results were so impressive "as to make it difficult to restrain enthusiasm within scientific bounds." None of the other writers experienced this difficulty, but spoke of their results in more moderate terms. Keating noted better results from the use of autogenous vaccines made from streptococci agglutinated by the patient's serum, than from the use of those to which patients exhibited skin sensitivity but no agglutinins. Thompson, Wyatt, and Hicks considered a patient suitable for treatment with vaccine or antigen when sedimentation rates were high and agglutination titers low. Delatour's best results were with autogenous vaccines from hemolytic streptococci recovered from various foci including stools, to which patients were skin-sensitive (no results given). Attempted "immunization" against hemolytic streptococci seemed rational and beneficial to Hartung who gave intradermal and subcutaneous injections of a stock filtrate of a seven day broth culture. This preparation contains more of the exotoxins and decomposition products than a vaccine, and requires no further sterilization. The patients of Rawls, Ressa, Gruskin and Gordon who were markedly sensitive to vaccines, tolerated larger doses when thyroid extract was given.

Vaccines were considered of limited value by others and their results disappointing.[450, 1029] Cohn noted definite permanent improvement of only one of 74 patients given vaccines for six months. One great fault of vaccine therapy is that too many patients are treated by vaccines only for long periods, and gradually drift into a helpless, hopeless condition when other measures might have been employed usefully.[264] "Some dramatic results" with antistreptococcal serum given in normal saline solution per rectum were noted by Willcox (no details). Warner made a detailed critique on the subject of vaccine therapy in rheumatism. The use of large doses of vaccine has not proved of value. Desensitization should be attempted with small doses and focal reactions in joints avoided. "The principles of Warren Crowe's treatment [small *descending* doses] are in the right direction." Warner suggested that desensitization by oral methods may be of value. Vaccine therapy "may yet come into its own when used with greater skilled care and knowledge than has accompanied its use in the past."

[Some of us find it difficult to understand why vaccines should be expected to cure this disease of unknown origin when we know of no infectious disease of known etiology cured by vaccine.—Ed.]

Foreign Proteins. Only passing approval was given this form of therapy.[254, 1029]

Chaulmoogra Oil. A preparation containing "90 per cent chaulmoogra oil, 10 per cent olive oil and 2 per cent benzocaine" was used by Smith, Blocker and Tumen in 15 cases of atrophic arthritis and 33 of mixed arthritis: in 87 per cent of the former and 55 per cent of the latter symptoms

disappeared. The oil was injected intragluteally eight times in six weeks. It was rather irritating; one sterile abscess formed and required aspiration.

[One of us, J. A. K., has given up this remedy because of the severe pain produced by the injections and because significant results were not noted.—Ed.]

Bee Venom. An old popular European notion is that rheumatism can be cured by bee stings. Several injectable forms of bee venom have been produced recently: apicosan, apicur, apisin, British bee venom, immenin. Forapin is an ointment of bee venom, salicylic acid and oil of mustard. Bee venom is an albumin-free sapotoxin allied to snake venom, combined with a poison similar to cantharides. It contains no formic acid. Bee venom is supposed to act as a foreign protein, as a counter-irritant, as a desensitizing agent, or through a histamine-producing action. Burt could not prove the last effect. He noted good results in cases under two years' duration. Of 200 cases so treated, results in 50 were analyzed: 32 per cent of the patients were "very much better," 18 per cent were "better," 30 per cent were unchanged, 20 per cent were worse. Bee venom therapy is "by no means specific" but "of definite value in certain cases." Apicosan was used by Kroner, Lintz, Tyndall, Anderson and Nicholls in the treatment of 100 patients: none was cured, 35 were markedly improved, 38 moderately improved. Relief was "definite and lasting" and sedimentation rates fell. From 6 to 52 intradermal injections were given within 1 to 14 months. Untoward reactions occurred twice: severe urticaria and cellulitis necessitating surgical care. "Bee venom is worthy of further consideration."

[Results were not compared with any control series treated otherwise. We understand that this therapy is no longer used in the clinic where the work was done. One of us, W. B., has had very disappointing results with bee venom therapy.—Ed.]

This work was published in January; in September Nicholls, one of the co-authors, published a pessimistic report on results in 27 cases of treatment, not with injectable bee venom, but with the actual sting of honey bees. Five patients stopped treatments because they were "very disagreeable" or produced severe local or general reactions. Twenty patients accepted from 53 to 1,434 stings within 3 to 18 months. Three patients were "markedly improved and had remained well one year later," five were slightly improved, five unimproved and seven became "very much worse." Minor reactions were common: severe itching, rash, focal reactions in joints, severe headaches. "Bee sting therapy had no constant or noteworthy effect. Results were so discouraging that we felt we were not justified in continuing this form of treatment."

The results of Douthwaite with bee venom were "most unsatisfactory," those of Reichart (with "Apis D3") were good in fibrositis, "not encouraging" in arthritis (no details given). According to Kersley [532] the popularity of bee venom is decreasing in England; many think of it now only as a method of counterirritation.

Diets. There is no "arthritis diet" per se. The dietary prescription for each individual should provide for optimal nutrition, relief of constipation, and an abundance of vitamins and minerals, and should avoid foods to which patients may be sensitive.[686] A diet with carbohydrate restrictions seemed so important to Davis that he recommended that food should be weighed and managed with much the same accuracy as in diabetes. "The patient should weigh his own food, otherwise he will not follow the diet." Davis also recommended the use of an unnamed "seaweed preparation" as the best source of minerals since "ordinary vegetables are often deficient in minerals." Such a complex regimen found no other support. The diet usually approved for thin arthritics was one rich in calories, vitamins, and vitamin supplements, and low in starches; for obese arthritics one with caloric restrictions.[952] Most arthritics need generous amounts of proteins. "Acid-fruits" are *not* harmful: their organic acids, e.g., malic and citric, are completely oxidized in the body and excreted as carbon dioxide and water. Fruits are highly valuable sources of vitamins and minerals. Buckley deemed it wise to cater to the idiosyncrasies "commonly met with" in rheumatic patients. Strawberries, rhubarb, apples or cider were suspected of being irritating, especially to fibrositic patients. Even more strongly did Pottenger stress the supposed importance of uncovering food sources of gastrointestinal allergy. In rheumatism the saying "One man's meat is another man's poison" is particularly true, according to Kersley. One rheumatic may thrive on a diet of orange and tomato juice, while another may have an exacerbation from a tomato. But "if all the foods that may increase rheumatic symptoms were removed from the diet nothing but water would remain."

[We cannot approve the emphasis laid on the factor of food allergy in cases of atrophic arthritis; it is neither common nor do we consider it important. Variations in articular symptoms are so common from day to day that it is easy to blame erroneously some food for the day's ill-feeling. Cases of atrophic arthritis with undoubted and repeatable articular exacerbations from foods are few and far between. —Ed.]

Vitamins. Vitamin B. Supplements containing this vitamin are recommended [254] to correct the vitamin B deficiency of arthritis, and to prevent "neuritis" which may accompany gastric achlorhydria.

[We have never noted true neuritis in any of our patients with achlorhydria. —Ed.]

Vitamin C. In an unstated number of cases Rinehart and his associates noted "distinctly encouraging" results from the administration of the sodium salt of cevitamic acid intravenously and vitamin C orally (no details given). Hare and Williams gave six patients a diet rich in vitamin C and low in chloride; "an undoubted clinical improvement" was noted by all six, but that of the two who received 15 mg. of sodium chloride daily was less marked. It was suggested that the low output of chloride may have in-

fluenced a loss of fluid around joints. Blood chloride levels were constant. Supplementary feedings with vitamin C were approved by Sherwood.

Vitamin D. In the last review brief comments were made on the "remarkable" results which Farley claimed to have noted in 27 cases of chronic arthritis from massive doses of vitamin D. Farley has continued his paeon of praise for this mode of therapy as, "a weapon effective in every type of arthritis, regardless of the state or advancement of the disease, a weapon so powerful that it often accomplishes dramatic results *in the end stages* [italics are ours.—Ed.] of arthritis, after practically all other means of therapy have proved of no avail." To 87 patients with "arthritis" he has now given from 50,000 to 1,000,000 U.S.P. units of vitamin D [ertron] daily: optimal doses, those tolerated without toxicity, varied from 150,000 to 500,000 units daily. "Every patient responded well to the management established, unfavorable results did not appear in a single instance."

[No details whatsoever were given regarding 84 of the 87 cases. Only 3 brief case reports were noted. No attempt was made to classify the types of arthritis treated. The reader is asked to accept the writer's practically unsupported word as to these wonderful results. The wording of the report is, to say the least, incautious, and the results are quite at variance with those reported by others including the originators of this form of therapy. Reports of this kind are bound to lead to serious disappointments by others, add to the cost of treatment, and may indeed lead to dangerous effects for patients.—Ed.]

In sharp contrast to Farley's report were two others, one by Steinberg and one by Abrams and Bauer. Steinberg generally gave 160,000 U.S.P. units daily to 29 patients with atrophic arthritis: "10 showed clinical improvement and 19 showed no improvement whatever." The influence of the vitamins on blood calcium and phosphorus was studied in 12 cases. No marked hypercalcemia developed. These doses first raised a low or normal serum calcium to a higher level, later the hypercalcemia decreased. Calcium levels in blood bore no relationship to symptomatic results: no untoward results occurred. "No specific virtue exists in such medication." From 80,000 to 160,000 U.S.P. units of vitamin D (Drisdol in five cases, crystalline vitamin in others) were given daily by Abrams and Bauer to 18 patients with atrophic arthritis. Subjective improvement, lasting through the period of treatment, was noted in eight cases, in only three cases was there objective improvement and in only one was it marked. When therapy was stopped the improvement was short lived. Significant reductions in sedimentation rates were noted in only five cases, in only two of which was improvement subjective and objective. Hypercalcemia (up to 16 mg. per cent) developed in 16 of the 18 cases. Toxic symptoms frequently occurred. It was concluded that massive doses of vitamin D are "of little or no value in altering the course of this disease. The general effects of the larger doses do not appear significantly different from those observed with the usual therapeutic doses, and do not justify the expense and dangers involved."

On the basis of their results as a whole, Abrams and Bauer are justified in their conclusions. But in at least one case (No. 286) a marked subjec-

tive and objective improvement occurred, lasted only a few weeks after medication was stopped, and recurred definitely but less notably when medication was resumed.

[Two of us, W. P. H. and A. J. K., have noted such an effect sufficiently often to recommend further consideration of this therapy as a research investigation, but not as a remedy suitable for general practice.—Ed.]

The use of cod liver oil, plain or with malt extract, in ordinary doses was recommended; if the oil cannot be tolerated, viosterol (irradiated ergosterol) or radiostoleum (5 drops t.i.d.) is used (Ellman).[282]

Additional Intestinal Therapy. Salol (phenyl salicylate) or guaiacol were recommended as "intestinal antiseptics."[233, 245] According to Douthwaite many patients exhibit an excess of gastric mucus, the result of chronic gastritis, which lowers the free acid in gastric juice. "If these stomachs be washed out with peroxide of hydrogen and water so that excess mucus is removed, a further test meal may reveal a normal acid curve." Some prescribed hydrochloric acid for patients with gastric hypo-acidity, but others[254] noted no dramatic results therefrom. Constipation should be controlled by diet, habit-time, abdominal exercises and massage. If necessary, an occasional high colonic injection, an enema of salt solution or small injections of oil can be used and are preferable to the habitual use of cathartics according to Keating. Repeated colonic injections are harmful.[245] White permitted the use of a mild laxative daily, cascara and oil, or heavy calcined magnesia. That preferred by others[40] was a full glass of tepid normal salt solution taken early in the morning. Assuming that a hepatic dysfunction exists in this disease O'Connor frequently gave calomel followed by a saline cathartic to "assist the liver in its detoxicating function." Such measures were approved by van Breemen: "It is well known that quacks frequently attain success in chronic rheumatism because they prescribe starvation diets and strong purgatives much more frequently and with greater skill than do medical men."

Miscellaneous Medicines and Other Substances. There is no drug known to have a direct influence on the joints in arthritis.[315] Hence the rôle of drugs is limited "but not unimportant."[282] For pain, aspirin (45 to 60 grains daily) was considered best, but one should "give enough." Antipyrine was recommended also. When pain is severe the occasional use of 1/10 grain of dilaudid with 10 grains of phenacetin seemed permissible to Douthwaite. Dilaudid is a morphine derivative, dihydromorphinone hydrochloride. For sleeplessness caused by pain 10 to 15 grains of aspirin at night with a sedative were given. For sleeplessness not caused by pain 15 grains of bromide with 10 grains of chloral flavored with syrup of tolu seemed preferable to barbiturates. To counteract the distressing fatigue of arthritic patients the use of elixir glycocoll (amino-acetic acid: glycine) "serves admirably" (Lautman), and Douthwaite found benzedrine sulfate "remarkably efficacious" (20 mg. in the morning and just after lunch but none after 2 p.m. lest insomnia be produced).

[The latter has an ephedrine or adrenalin-like effect, objectionable to some. The matter of dosage must be individualized, that amount being used which will relieve fatigue but not produce nervousness or insomnia. It should be used occasionally, not habitually, and with discretion.—Ed.]

Thyroid extract. In cases of atrophic arthritis associated with hypothyroidism (these are not common) the use of thyroid extract has been considered useful: "Remarkable reduction of joint swelling and an immensely improved range of joint movement frequently result" (Ellman). But Rawls and his associates were not impressed with it. "Only 20 per cent of patients with markedly active rheumatoid arthritis showed improvement." Many patients could tolerate only small doses, and in some cases it had to be discontinued. Some patients noted improved appetite, euphoria and "increased resistance to infection." [How measured?—Ed.] But joint symptoms and metabolic rates were not affected even though the latter were subnormal.

Insulin. Ellman gave again his scheme of insulin therapy to counteract anorexia and loss of weight (5 to 30 units daily for two to three months).

Progestine. To three patients (two with "primary chronic polyarthritis," one with "secondary osteoarthrosis deformans") whose articular symptoms were markedly benefited during pregnancy Touw and Kuipers gave "2 c.c. progestine (10/E)" intravenously daily for 10 to 11 days during the second two weeks of the intermenstrual period. After two or three such courses 2 of the 3 patients noted marked relief of articular symptoms; the third patient received only one course and was less notably benefited. Pregnyl ("1,000 E. daily") was ineffective.

[One of us, W. B., has given progynon 10,000 rat units biweekly for months in cases of atrophic arthritis without effect. In two of these cases an additional 10,000 rat units was given daily for 9 and 10 days respectively also without effect.—Ed.]

Amniotic fluid concentrate. This substance when injected intraperitoneally is said to prevent or minimize formation of adhesions. According to Schimberg its intra-articular injection hastens a defense-repair mechanism within joints, successfully prevents the formation of new adhesions after closed manipulation of joints, is a valuable prophylactic after arthrotomy, and produces no untoward reactions. Results obtained in intra-articular fractures were "impressive," those in selected cases of atrophic arthritis and persistent joint effusion were "encouraging." In six cases of subacute atrophic arthritis effusions were withdrawn and replaced with a larger volume of the concentrate on from two to seven occasions: results were "satisfactory," the symptoms cleared up, and during the period of hospitalization the improvement was maintained.

[One of us, M. H. D., obtained some amniotic fluid concentrate (amfetin); but since it appeared to contain little or no protein and no carbohydrate, it was regarded as biologically inert.—Ed.]

Lactic acid (intra-articular injections). Encouraged by his results noted under "Treatment of traumatic arthritis," Waugh made similar injections in five cases of atrophic arthritis, since the synovial fluid was abnormally

alkaline ("pH 8 and over"): "All derived much benefit." One case in which the result was especially gratifying was reported in detail.

Procaine. Considerable analgesia has presumably resulted from intra-articular and periarticular injections of procaine in various arthritides. Tarsy used procaine hydrochloride, 1 per cent solution, in most cases, eucupine oil in others. Results were "not as good" in the progressive infectious arthritides as in the degenerative or traumatic forms, but "exceptionally good results" were noted in "several" cases of atrophic arthritis despite the fact that "in the main, results have not been gratifying."

Miscellaneous. The supposed indications for and value of the following were discussed: arsenic, strychnine, quinine, calcium, iodine, and calcium or ammonium orthoiodoxybenzoate.[238, 254, 282]

[Editors of symposia on rheumatic diseases frequently ask physicians to write on the use of drugs for these conditions. Despite the fact that the value of drugs is limited, the physician writing such a chapter often attempts to make a "decent showing" in their behalf, with the result that he is in danger of recommending a whole pharmacopoeia rather uncritically, if not actually *con amore*. The recommendations of an "authority" under such circumstances too often perpetuate false ideas on the value of these medicines in arthritis. Patients are then likely to use them for a long period to the exclusion of much more important measures.—Ed.]

And now for some pharmaceutical "step children."

Causalin (aminodimethyl-pyrazolon-quinoline-sulphonate). Kimble was the year's torchbearer for this remedy. In 36 of 56 cases of "chronic nonspecific arthritis" treated therewith either "marked improvement or complete remission of symptoms" occurred.

Arthranol (amino-salicyl-phospho-benzoyl-iodide). Mingled with some philosophy and morality was the recommendation of Stern and Kurland for this substance: "Our results were over 90 per cent successful in our arthritics."

[One wonders whether the "before and after photographs" showing improvement in articular function and posture were taken really before and after a course of treatment or at the same photographic sitting.—Ed.]

Subenon ("calcium double salt of benzoic and benzyl succinic acid"). With this substance, Leir treated "all types of arthritis." He stated: "Within a comparatively reasonable time after subenon was administered, a large percentage showed varying degrees of improvement, in some cases exhibiting a restoration that was most gratifying." Supposedly corrected was some vague gastrointestinal dysfunction presumed to cause arthritis.

Arthox ("sulfiodoxygenia"). This "patent medicine" once contained sodium salicylate and many other substances supposedly good for arthritis, rheumatism and muscular aches. Later, it was found to contain as its essential ingredients sulfuric acid, sodium iodide, flavoring substances and probably colchicine. The manufacturers must have run out of salicylates! In other words "when one buys a 'patent medicine' one buys a name and not a thing."[140]

Transfusions; hematonics. For cases of significant anemia large doses of iron and transfusions have been recommended. According to Atsatt and Ussher the anemia should be vigorously combated (by the usual hemogenic agents plus liver extract as needed) because "ofttimes the whole success of treatment may hinge upon the up-building of the blood picture." Douthwaite considered the treatment of the anemia "a simple matter seldom needing more than the administration of iron in adequate doses." Freshly prepared Blaud's pills (50 grains daily) were "highly effective" but sometimes produced indigestion and constipation. Blood transfusions rarely were considered necessary. Hartung's view was that, unfortunately, the anemia is caused mainly by the disease itself, so that the hemoglobin can be raised only with the greatest difficulty. "Transfusions likewise have only a temporary effect but are invaluable in giving the patient that lift which sometimes means the onset of recovery." They were considered "extremely useful" by Thompson, Wyatt, and Hicks who gave 198 of them to 48 patients (average of 4 transfusions per patient, each 300 to 600 c.c., at intervals of two to six weeks). "Improvement" was noted in 66 per cent of cases; subsequent sedimentation rates were frequently halved.

[Although slight or moderate reductions in hemoglobin and erythrocytes are common, marked deficiencies are rare. "There is no foundation for the suggestion that anemia may be the causal factor" (Shackle). Under the mistaken idea that "If we can only build up the system and correct the anemia, the joints will take care of themselves" too many physicians treat the anemia strenuously, usually without notable success, and neglect more important measures. It is more correct to say, "Treat the arthritis and the anemia will care for itself." Of course significant anemia should be treated, but dramatic results are not to be expected.—Ed.]

Sulfur. This remedy for arthritis has about run its span of favor. Nothing good was said of it. "The results are essentially nonspecific" [254] and "disappointing." [952] "Sulfur injections do not seem to fulfill claims made for them." [564] The Council on Pharmacy and Chemistry [226] of the American Medical Association after reviewing 42 articles thereon, accused the proponents of this therapy for arthritis of having been uncritical in their judgment, careless in the details of their cases, negligent about the proper typing of the cases of "arthritis" under treatment, and not sufficiently sure of the indications, contraindications or proper dosage of sulfur. "Not one of the leading arthritis clinics of the United States has adopted the use of sulfur in the treatment of arthritis so far as can be determined." The Council concluded, "It is unsuited for experimental use except in institutions, or under other conditions in which its effects may be followed intelligently and accurately for prolonged periods."

Gold Salts: Chrysotherapy. Several new English but no detailed American reports on this form of treatment appeared. Although the treatment is empirical, it was called "the greatest step forward in therapeutics since the disease was first described" (Douthwaite), "a method which gives results incomparably better than any obtained hitherto" (Stone).[918]

Preparations. The gold salts used in these reports were myochrysine (van Breemen), solganol B (van Breemen; Stone), allochrysine (Stone), sanocrysin (Secher), and a new one, parmanil (Bayer) (Hartfall, Garland and Goldie).

Indications. Suitable for treatment are any active cases of atrophic (rheumatoid or chronic infective) arthritis with no obvious renal or hepatic disease or history of purpura.[253, 918]

Contraindications. The presence of definite renal or hepatic disease, a personal or family history of purpura or other blood abnormality (except mild secondary anemia) was considered an absolute contraindication for this treatment.[283, 284, 918]

Results. Two English and one American commented unfavorably. Willcox said, "I do not like to use gold salts," because of the risk of complications. Another physician [539] wondered whether the only real use for gold in this disease was the transference of gold from the patient's pocket to that of the physician. The results of Thompson, Wyatt and Hicks were "disappointing" (no details given). But van Breemen was "very satisfied" with results in about 300 cases: "The results surpassed those of any other therapy." However, he considered it "extremely dangerous." Without giving details of his own results Stone considered gold therapy "unquestionably the most valuable therapeutic measure discovered so far. Dramatic cures are sometimes obtained, while relief of pain, swelling and stiffness is so common that the efficacy of gold can scarcely be doubted." Despite these good results Stone also called it "a dangerous drug." Of patients so treated pains may begin to lessen after only a few injections or not until over 1 gm. has been given, sometimes not until two or four weeks after the first course.[253] Sedimentation rates generally begin to fall after two or three injections, but there is often an initial rise after the first month of treatment.[283]

A serious criticism of almost all previous reports has been that no observations on controls were made. These have been made now by Ellman, and Ellman and Lawrence. Ellman gave injections of gold to 24 patients with "infectious arthritis" and of almond oil to 14 arthritic controls. Beneficial effects were noted by both groups but especially by those receiving gold: three of the latter but none of the controls were cured. Later Ellman and Lawrence treated three groups, of 20 patients each, by sterile oil, small doses of gold (maximal dose 100 mg.) and large doses of gold (maximal dose 200 mg.). The records of subjective improvement were fortified by measurements of actual articular sizes and of sedimentation rates.

Results are given in table 2.

Thus gold, in large and small doses respectively, cured 10 and 6 times as many as the oil injections. Hence it was concluded that the effects of gold were not merely psychic, and that chrysotherapy was a distinctly superior form of treatment. "The effect of gold is to hasten the course of the disease by producing first an aggravation, then a gradual improvement so that

TABLE II

Results in Percentages

Result	On Large Doses of Gold (20 Cases)	On Small Doses of Gold (20 Cases)	Controls on Oil (20 Cases)
Cured	50	30	5
Improved	45	60	65
Not improved	5	10	30
Joint swellings reduced	81	79	16
Sedimentation rates reduced to normal	74	40	15

the inactive stage is reached in one year instead of in 20 to 30 years as is often the case without gold."

Having previously treated the enormous number of 1200 cases with various gold salts, Hartfall, Garland and Goldie used a new "equally effective" and less toxic preparation, parmanil, in the treatment of 50 patients, 21 of whom had had the disease five or more years.

Parmanil (Bayer) is an oily solution for intramuscular use, the methyl glucamide of auro-thio-diglycollic acid; its total gold content is 50 per cent. Weekly injections were given, beginning with a dose of 25 mg. and increasing to 100 mg.; total dose for a course was 600 mg. given in about 12 injections. One course was given to 31, two to 19 patients. Of the 50 cases, cures resulted in 4 per cent, marked improvement in 84 per cent, moderate improvement in 6 per cent, slight improvement in 2 per cent, none in 4 per cent, deaths in none. These results were compared with those noted in 690 cases treated with older gold salts, in which cure resulted in 10 per cent, marked improvement in 57 per cent, moderate improvement in 13 per cent, slight in 6 per cent, none in 11 per cent, death in 3 per cent (19 cases). Thus although cure was achieved in only 4 per cent by parmanil and in 10 per cent by other salts, parmanil produced marked improvement in many more cases. "The results with parmanil are as good, if not better" than those from four other gold salts (lopion, solganol B oleosum, crisalbine, myocrysine or myochrysine). The doses of parmanil were smaller than those of some salts, about equal to those of lopion: the latter produced no cures, marked improvement in 41 per cent of cases, as compared to cures or marked improvement in 88 per cent of cases in which parmanil was used. Toxic reactions from parmanil were slight in 14 per cent, moderate in 6 per cent, severe in 6 per cent (total 26 per cent) and absent in 74 per cent of cases. Compared to reactions from other salts these figures indicate that parmanil is perhaps the least toxic of the gold salts.

[Although the total percentage of toxic reactions from parmanil was lower than that from other salts, the percentage of *severe* reactions was about the same. Thus severe reactions occurred from crisalbine in 5 per cent, lopion (large doses) in 4 per cent, solganol in 2 per cent, myochrysine in 6 per cent, parmanil in 6 per cent, lopion (small doses) in 3 per cent of cases so treated.—Ed.]

General plan. The plan was to give injections of gold every five to seven days; initial dose was 10 mg., subsequent doses 20, 50 and 100 mg., maximal single dose 100 mg., total dose for one course 1 gm.[918] Douthwaite gave, in acute cases, 10 mg. for each of three doses, then if no reactions occurred, 50 mg. for each of six doses, then 100 mg. doses thereafter until 1.5 gm. of solganol or myochrysine was given, or 2 gm. of allochrysine; in less acute cases six or seven doses of 50 mg. each, thereafter 100 mg. each dose. The schemes of Ellman and Lawrence were different. Patients given the "larger doses" received 10, 50, 100 and thereafter 200 mg. each dose

up to a total of 2.5 gm. But those given the "smaller doses" received 10, 20, 40, 75, and thereafter 100 mg. each dose until the sedimentation rate fell below 10 mm. (1 hour). To accomplish this the weekly doses were often continued uninterruptedly for nine to twelve months. According to Ellman and Lawrence no harm results from prolonging the first course no matter how large the total dose of gold given, provided the sedimentation rate remains high and the leukocyte and platelet counts are satisfactory. "The present practice of limiting the first course to one gram is likely to lead to numerous failures." Six weeks after the end of the first course, they began the second course, this time with 50 mg. as a maximal dose.

The number of courses required was "always two, generally not more than three or four" (Stone), "usually four to six" (Douthwaite). Intervals between courses were two to three months (Douthwaite), three months (Stone), six weeks (Ellman and Lawrence).

Toxic reactions. These are common, occasionally serious or even fatal and provide the great drawback to chrysotherapy. Because of them the drug was called even by its proponents, "extremely dangerous." These reactions were discussed in some detail in previous Reviews [4, 5] and include giddiness, headache, vomiting, abdominal pain, diarrhea, focal reactions in joints, fever, stomatitis, jaundice, albuminuria, various skin reactions from herpes to exfoliative dermatitis, colitis, proctitis, rarely neuritic and ocular lesions (conjunctivitis, phlyctens). The most disturbing reaction is exfoliative dermatitis, the most severe is agranulocytosis.[214, 253, 283] Use of the drug should be stopped if the following occur: erythema with slight fever (this may be a forerunner of exfoliative dermatitis), significant albuminuria, stomatitis, dermatitis of squamous or exfoliative type, hepatitis or jaundice, blood dyscrasias (purpura hemorrhagica, agranulocytosis, aplastic anemia, marked fall in blood platelets [348]). Blood dyscrasias generally occur, if at all, late in treatment. Agranulocytosis must be considered an idiosyncrasy, not a sign of metallic toxicity. According to Secher most of the reactions are not due to metallic intoxication but to toxins liberated from the affected tissues themselves. In four of their 60 cases Ellman and Lawrence noted stomatitis, in six exfoliative dermatitis, in one case agranulocytosis.

Treatment of toxic reactions. This is purely symptomatic. Sodium thiosulfate is now considered useless.[283, 284, 348]

Prevention of toxic reactions. There is no known certain method of preventing them. One should adhere to the contraindications, examine skin and urine weekly, make blood counts (especially leukocytes and platelets) [348] at least every two or three weeks, and discontinue, at least temporarily, the injections at the first sign of any significant reaction, some say at the first sign of any reaction however slight.[918] Calcium gluconate is considered of no prophylactic value. If the drug is stopped on the appearance of a metallic taste, stomatitis may be avoided.[214] Eosinophilia is said to precede dermatitis, but usually too closely to be a useful warning.[214, 849] But eosinophilia is a fairly frequent feature of the disease itself and not just a sign of gold toxicity although it is aggravated by chrysotherapy.[283, 284] A rather sudden change from leukocytosis to leukopenia may signify impending dermatitis.[214]

Since the severe toxic reactions generally occurred, not when sedimentation rates were high, but toward the end of a course when rates were no longer high, it appeared to Ellman and Lawrence that patients with an elevated rate were more immune to toxicity than those with normal or almost normal rates. Hence they recommended that the dose be reduced to 30, 10 or even 5 mg. when sedimentation rates approach 10 mm. (1 hour). Secher claimed that the severe toxic reactions can be prevented or checked by the vigorous use of vitamins A, B and C. Beginning a few days before gold was given he gave daily vitamin A 20,000 international units, vitamin B 750 to 1500 international units, vitamin B_2 375 to 750 Krieger Lassen units, vitamin C 2500 international units. "The results so far have been excellent"; no difficulty of any kind occurred during treatment in 150 cases.

[These doses of vitamins would cost about 15 to 20 cents daily. If they really will prevent serious toxicity from this therapy they are certainly worth it.—Ed.]

Vasodilators: Histamine, Choline. The use of histamine by injections was considered by Douthwaite to be of definite value in certain cases with vasomotor changes but little deformity. The effect of each injection lasts only from a few hours to two or three days. Nevertheless sometimes "it may act like a charm; I have known patients who had become, one might say, histamine addicts so great was the relief they received." But in most cases the results are "transient and disappointing." Histamine was used by Stormont as an ointment, "imadyl," with presumed benefit.

The use of mecholyl iontophoresis (acetyl beta methylcholine chloride) was approved in various types of arthritis, including atrophic (Bredall). Neuberger and Scholl (1937) reported that subcutaneous injections of acetylcholine prevented the ankylosis and muscle atrophy which normally follows experimental immobilization of the limbs of animals. As a result of experiments on 12 rabbits Harvey could not confirm this report: the drug did not prevent the results of immobilization.

Sulfanilamide. Of 13 patients given sulfanilamide by Koerner and Poulton seven noted "improvement." But the results were not striking. From 25 to 50 grains daily were given for three or more weeks. Several patients treated by Finn seemed to be benefited, especially those with the more acute condition (no details). But Simmons and Dunn were "not impressed with its value in atrophic arthritis" (no details). Bauer and Coggeshall gave large doses to 10 patients without affecting sedimentation rates or the course of the disease: "the agent responsible for rheumatoid arthritis is not susceptible to this type of therapy." In two cases of rheumatoid arthritis nonfatal agranulocytosis developed after seven and 30 days of this therapy.[23,645]

Bile Salts; Bilirubin, Artificial Jaundice. For years certain physicians have tried to connect atrophic arthritis with some vague hepatic deficiency, or perhaps a hepatic dysfunction in the nature of a failure of the detoxifying function of the liver. But the idea has been incapable of proof since no

significant pathologic lesion in liver has been noted and a few studies with different tests of hepatic function have shown no consistent hepatic insufficiency (Watson, 1928; Rawls, Weiss and Collins, 1937). However, this notion is the basis of the French concept of "arthritism" [84] and the possible connection was mentioned in passing by current writers.[335, 720, 791] Recent observations on the ameliorating effect of jaundice on atrophic arthritis seemed to suggest, perhaps more definitely than heretofore, that there was some direct or at least indirect connection between atrophic arthritis and the liver. Hench [430,432] therefore made various attempts to reproduce the analgesic effect of spontaneous jaundice by using bile and related substances. No significant results were noted by him from the use of bile salts (glychotauro, oxgall), or synthetic bile salts (decholin, sodium dehydrocholate) given orally, large amounts of human bile given by stomach tube (up to 2,600 c.c. in one day or 7,650 c.c. in 10 days) or ordinary liver extracts. A few patients were given one to four transfusions of fairly large amounts of highly jaundiced blood (up to 800 c.c. of blood containing 21 mg. of bilirubin per 100 c.c.). One patient accepted experimental jaundice induced by toluylenediamine. No significant effect on joints was noted from these procedures. For reasons stated in his paper injections of bilirubin were not given.

Later, Thompson and Wyatt noted that the intravenous administration of bile salts alone (decholin, 2 gm. daily for 9 to 12 days) had no effect on atrophic arthritis, nor did injections of bilirubin alone (10 to 15 mg. per kilogram daily for several days) in three cases. But they reported that injections of bilirubin (10 mg. per kilogram) and "decholin" (40 mg. per kilogram) in combination produced an ameliorating effect "which apparently duplicates the effects" of spontaneous jaundice. The injections produced no significant toxicity and no definite evidence of hepatic or renal dysfunction. They were given to 10 patients daily for 7 to 11 days. Definite icterus and hyperbilirubinemia were produced (concentrations of serum bilirubin rose to between 19 and 35 mg. per 100 c.c.). After several doses articular pain and swelling diminished in varying degrees and for variable periods (in one case for 5 months, in another for 5.5 months, in others for 2, 1 and 1 months respectively). Five patients were still free of pain at the time of the report. Jaundice had disappeared from 14 to 23 days after the last dose. Five months after the first report Thompson and Wyatt [951] noted the further effects of this form of artificial hyperbilirubinemia in a total of 16 cases in each of which an average of nine doses of the bilirubin-decholin mixture (from 7 to 12 injections) had been given. Of the 16 patients 14 experienced variable amounts of relief (analgesia and diminished articular swelling). Eight patients had "short" remissions (5 to 45 days), six had "long remissions" (2 to 13 months). The relief was complete in some cases, partial in others. Two patients noted no relief. Results bore no direct relationship to the degree of induced jaundice. Thompson and Wyatt concluded that it was possible to inactivate atrophic arthritis in this manner

more rapidly than by any other measure, and that the inactivating effect of this "artificial jaundice" was similar to that from spontaneous jaundice.

Hench was unable to corroborate this work in toto. To 11 patients with atrophic arthritis (and one with primary fibrositis) he gave 12 to 20, in some cases 25 to 30 daily intravenous injections of the bilirubin-decholin mixture. Rather intense degrees of visible jaundice were induced by daily doses, generally of 15 mg. per kilogram of bilirubin and 40 mg. per kilogram of decholin. Among the 12 cases little or no relief was noted in five, short incomplete remissions resulted for a few days only in six; one patient had a rather complete remission of symptoms which lasted only three weeks, the longest, most definite effect noted. Three slight changes in technic made by Hench seemed of possible significance to Thompson, but insignificant to Hench because results were no better when the differences were corrected. Hench concluded that by this means an obvious and apparently harmless bilirubinemia or "artificial jaundice" can be produced, the effects of which are not nearly as striking as those of spontaneous jaundice.

[In its present form the procedure is impractical, expensive, rather laborious, and inconstantly and incompletely effective. It is certainly not a practical "control of arthritis"[1052] and should be considered strictly a research procedure. But the fact that the disease can be modified at all by such a novel and unorthodox method seems significant and affords further evidence that the disease may some day be made rapidly "reversible," at will. The work offers a wide field for speculation as to the possibility of discovering the agent responsible for the remissions induced by jaundice and utilizing it in the field of therapy.—Ed.]

The fact that jaundice should beneficially affect rheumatic patients seemed rational to Najib-Farah. Having discovered (1934) pneumococci in cultures of the blood of a patient with subacute rheumatic fever, he concluded that rheumatic fever was caused by pneumococci. He more recently has interpreted the bilirubinemia, which occurs not infrequently in pneumococcic and typhoid infections, not as evidence of impaired liver function but as a protective mechanism designed to overcome infection. According to him[693] bilirubinemia plays an important rôle in the processes of defense and immunity of the organism.

[It is reported[967] that jaundice affects 5 to 10 per cent of cases of lobar pneumonia in whites, a much higher (78) percentage of negroes. The lighter form of jaundice is said to have no significance, the deeper forms are reputed to be associated with toxic hepatitis and a grave prognosis. Were Najib-Farah's conception correct would not the prognosis be better in the presence of severe jaundice, and were acute and subacute rheumatism due to pneumococci would not sulfapyridine be highly effective?—Ed.]

Cystein. Shipton and Parr suggested that the beneficial results of jaundice and pregnancy might be related to retention or increased formation of one of the amino acids, perhaps cystein, during these states, also that the beneficial effect of operative procedures on atrophic arthritis may result from excessive autolysis of tissue protein, the sources of amino acids in the body being digested food protein, and autolysed tissue proteins. Hence an amino acid, histidine, was first given to arthritics (number unstated); "only one case out of three" was benefited. But when intramuscular injections of cystein (0.2 gm. daily) were given in two severe

cases of atrophic arthritis with marked skin atrophy, a "rapid and definite effect" was seen.

[The results are not very impressive; the first patient was given two periods of starvation of four days each just before administration of cystein was begun, and although "dramatic improvement" occurred it was deemed necessary later to commence gold therapy. In the second case also cystein was used with other measures. —Ed.]

Rest and Movement. Rest was called "the keystone of treatment" [539] and, "the most important single factor in treatment" [686] but one which should not be overdone. The patients should rest prone one hour after each meal with joints in the position of least strain. This can best be done by the use of splintage in light plaster shells.[539, 758] Rest in these moulds relieves pain and reflex muscle spasm and prevents deformity therefrom.[918] But complete rest must not be continued for more than a few (at most seven) days.[539] Prolonged complete rest is as dangerous as the advice often given to patients to "walk it off" or "keep about at all costs." An adequate range of articular motion must be maintained even during rest to sustain and improve muscle and joint function. Joints should be exercised within limits of their tolerance. Both rest and exercise should be prescribed in exact doses. Bradford outlined a system of exercises useful for bedridden as well as ambulatory patients; they should be instituted long before the patient is ready to get out of bed.

Physical Therapy. A great many physicians know little or nothing about physical therapy, others regard it as a not quite respectable stepchild of medicine. To raise physical medicine to its proper status is the aim of the American Academy of Physical Medicine and the American Congress of Physical Therapy. The ideals of these organizations were well stated in addresses by their Presidents Lowry and Krusen, respectively. They propose to promote proper teaching of physical medicine in medical schools, to combat unjustifiable claims, promoting at the same time valid claims; they seek to avoid commercial taint, to establish physical medicine on sound principles. Krusen made certain recommendations designed to improve the scientific reports of physical therapists. Such therapists should avoid the spectacular, avoid half-truths and overenthusiasm, and correct the inadequacies and inaccuracies too common to the literature of their specialty. Brief general articles outlined the technic, indications and contraindications for the various types of physical therapy [63, 64, 238, 551, 755, 756] and their physical (Taylor) and physiologic basis (Hill). Rather than apply these methods haphazardly and unintelligently physicians not trained in their administration, should refer patients for treatment to those who have been trained, but both physician and physical therapist should coöperate closely.[657] Physicians should try to select the form of therapy most suitable for each patient and should review their patient's condition at least after every 12 treatments to see whether the therapy should be changed to get better re-

sults.[64] Patients should be taught as supplements the simple inexpensive methods available for use in the home.[758] The physiologic effects of heat were noted,[63] also indications for the various types of light therapy (Eidenow). The simple infra-red lamp is "the best source of heat (Krusen)."[551]

The technic of contrast baths differs in various clinics: in many the alternating applications of hot and cold were given empirically for one minute each. Pennington used applications of three minutes each but considered them unsuited for patients with impaired peripheral circulation. Woodmansey, Collins and Ernst made an interesting study on the physiologic responses of different "normals" and patients with atrophic arthritis to contrast baths of different lengths.

Temperatures of the hot water were from 107 to 113° F., of the cold water, from 47 to 55° F. The time of the hot and cold applications was changed about to note what combinations induced the optimal response in peripheral circulation. Changes in the skin temperatures of extremities were recorded before, during and after the treatments. Ten healthy males produced the best type of circulatory response, skin temperatures went upward rapidly in a remitting or steplike fashion, indicative of rapid adaptability. It was found that when the common (one minute hot and one minute cold) technic was used, even the most responsive normal subjects failed to respond satisfactorily, the alternating periods were too short. Sometimes the technic resulted in an actual composite fall rather than rise in skin temperature. Responses were satisfactory with five minutes in hot and five minutes in cold water, and with seven minutes in hot and three minutes in cold, but the use of six minutes in hot and four minutes in cold water was the most comfortable for patients and gave rise to the best warming effects. Some healthy women and patients with atrophic arthritis responded abnormally to this scheme. In cases of active severe arthritis the "worst responses" were encountered: temperature curves revealed practically no local vascular reactions and a progressive cooling rather than a net warming of the extremity.

Since no male arthritic patient exhibited poor reactions, no evidence was obtained to suggest that atrophic arthritis is grafted on a preëxisting vascular dysfunction. The sluggish adaptability of peripheral circulation in arthritic men is the result, not the cause of the disease. Many "normal" women and most of the women with atrophic arthritis studied exhibited poor adaptability, i.e., a poor vascular response to the contrast baths. The preexistence of an inherent vascular defect or poor adaptability may increase one's susceptibility to atrophic arthritis or may favor a graver form of the disease, but it is not the primary cause of the disease in either sex. However, the greater incidence of vascular deficiency in women may account for the greater incidence of severe atrophic arthritis in that sex. Woodmansey, Collins and Ernst were unable to distinguish so-called primary rheumatoid arthritis from "infective arthritis" by these reactions. They suggested that "primary rheumatoid arthritis" is not a different disease but is merely rheumatoid (i.e., infective) arthritis in a female who already possessed a constitutional vascular defect (sluggish peripheral vascular reaction). Disease brings the preëxisting vascular failure into greater prominence.

[This is a useful, practical piece of research, undramatic but clear and concise, and typical of the kind of research in physical medicine of which much more is needed.

Krusen at The Mayo Clinic has corroborated this work in part. Many arthritic patients responded less satisfactorily to the one minute—one minute technic than to longer alternating periods. But his preliminary observations seem perhaps to indicate differences in the vascular responses of Americans and the English (which tourists have long suspected!). His normals and arthritics exhibited optimal adaptability to either a four minute hot, one minute cold, or to a four minute hot, two minute cold regimen.—Ed.]

Ultraviolet irradiation was strongly approved [64, 273, 274] and considered by some [450] more useful and "curative" than infra-red rays. Contraindications to heliotherapy are febrile arthritis, the appearance of general or local reactions, and the coincidental presence of active tuberculosis, myocarditis or general debility.[952] The supposed "specificity" of short-wave diathermy and its superiority over long-wave (ordinary) diathermy were argued by several [172, 173, 236, 731, 894] but denied by others [445, 447, 448, 553, 734, 943, 1018] who found no effect from short waves except the heat. But it was agreed that it was a most effective form of deep heating and gives results not readily obtained by other forms of heat; e.g., after 20 minutes application of short-wave diathermy to a hip joint the temperature of urine was 101° F. It produces a deeper, more uniform heat and is more readily applied, but the dosage is more difficult to control.[553] Studies in vivo showed that it produced more heat in muscles than in bone marrow [734]: it produced in vitro temperatures hotter in fat than in other tissues.[943] Galvanic and sinusoidal currents are useful in preventing muscle atrophy.[444, 877, 918]

Paraffin baths (wax at 130° F.) and mud packs (at 110 to 125° F.) can be given so hot because of the low conductivity of their heat.[755, 993] When not overdone their dehydrating effect is soothing, but patients may overestimate their value.[683] The various forms, rationale and physiologic effects of hydrotherapy were described.[19, 43, 211, 463, 881, 954] Described also were the optimal technic for hot and cold baths (Holmes; Pennington), the value of hot-water fomentations (Phillips) and of foam baths ("useful for fat arthritics" according to Hill), an improved type of Hubbard tank for underwater therapy (Currence), an inexpensive homemade whirlpool bath suitable for arms and legs (Boynton). Brine baths may stimulate circulation through some osmotic effect on skin; they are useful in chronic, but not in subacute, atrophic arthritis (Neligan). The deep or reclining immersion bath in conjunction with undercurrent douching or manipulative exercises is most useful in quiescent atrophic arthritis, according to Copeman [211] and Thomson,[954] but should not be used in any case of infective or true rheumatoid arthritis with the "slightest sign" of clinical activity: their skins and joints are too sensitive to it, and they may react poorly even to the mildest hydrotherapy.

The advantages of spa therapy were stressed.[18, 463] The waters contain no "specific" for arthritis, their medicinal ingredients are merely adjuvants; heat is the important factor plus the advantage of removing the patient from his home to a new environment.[264,756] Because it is often too ex-

hausting, treatment at spas and resorts may be less desirable in active cases than the more restful services available in hospitals or sanatoriums.

A list of approved American schools for physical therapy technicians, the standards required for them,[26, 225] and a scheme for the organization of a physical medicine unit in a teaching hospital were published.[1048]

Occupational Therapy. This form of treatment teaches arthritic patients interesting and even profitable ways of increasing joint and muscle function and possesses marked psychologic and remedial value. It is a specialized branch of physical medicine. The scheme used by the Department of Hospitals, New York City, was described. Various methods used in occupational therapy were outlined (Copeman; Merritt). Bradford stated that, although valuable, occupational therapy should "not be trusted for specific improvement, because in his interest in creating even a basket or a rug, a patient will work within the limits of joint motion and will forget to increase these limits." A survey of approved American schools of occupational therapy was made (Council on Med. Ed. and Hosp.). An association of occupational therapists has been organized in England.[718]

Roentgen-Rays, Radium. Deep roentgen therapy was considered "invaluable" in the later stages of atrophic arthritis; reduction of pain and swelling may be accomplished (no results given). Use of thorium X was noted.[532] Injections of water impregnated with radon were valueless.[444]

Fever Therapy. Fever therapy was considered of some value by Snow (no details) and by Ferderber, who noted "improvement" in 11 of 28 cases classified as chronic atrophic, acute infectious, chronic infectious and rheumatoid arthritis. This therapy seemed of little value to others (no details; Thompson, Wyatt and Hicks). In Paul's 28 cases, results of treatment were "excellent" in 11 per cent, good in 43 per cent, insignificant in the rest. Others [40] disapproved of the usual sessions of fever, but approved the use of "mild sessions" (101° F. for one hour). No details were given.

Sympathectomy. Atrophic arthritis was not thought by Adson to be generally suitable for sympathectomy: "unfortunately the results are not consistent."

Hysterectomy. Solomons concluded that hysterectomy is indicated in a few rare cases of atrophic arthritis. He reported the case of a woman, aged 40 years, whose arthritis of some years' duration became worse after the birth of her last baby. There was some leukorrhea; menstruation was "heavy." The cervix was normal. "Therefore the major operation was decided on, and hysterectomy with double salpingo-oöphorectomy was performed." The uterus was essentially normal histologically. "The patient has been well and free from pain and deformity since operation."

[It would have been interesting to know what effect, if any, this patient's previous seven pregnancies had on her arthritis. The postpartum exacerbation of her disease was similar to that noted in the case of De Sa in which hysterectomy also was done. It is not likely that the removal of the uterus per se influenced her disease; she probably experienced the nonspecific effect which may follow any surgical procedure. —Ed.]

Nonsurgical Orthopedic Methods. The most important factor in preventing deformities is to reduce muscle spasms by resting the part for short periods in light splints with the joint in the optimal position.[124, 160, 539, 583, 759] The optimal position for each joint was listed.[160] "If a patient with a simple distortion of one joint is not protected, serious deformities of multiple joints will certainly follow" (Stump). Splints must be removable to permit the application of heat and some joint motion. Fisher preferred light metal splints to plaster. Casts of cellulose compound are "superior to plaster of Paris splints"; they are much thinner, lighter and less expensive (Joplin). To shoulders affected with pain and muscle spasms Kuhns applied plaster abduction splints but Capener applied adjustable metal abduction splints. Osgood stressed the importance of correct body mechanics in preventing deformities.

Surgical Orthopedic Methods. These aim to correct deformity, restore motion, and stabilize painful or disorganized joints. The technic of the various procedures was described (Lewin). Before submitting to them the patient's joints must have been free of active inflammation for "a long period," and he must have enough physical strength, morale and financial resources to endure the long postoperative care in the hospital and the later care (Osgood).

1. Manipulation under anesthesia. In suitable cases this may be very valuable when done by skilled hands. It may shorten treatment notably but it should never be done to actively diseased joints.[317, 539, 583, 759] "The watchword is gentleness." Osgood considered it "of limited usefulness."

2. Capsulotomy. This may be required to correct some knee deformities but is not likely to be successful if there is already much damage to the articular surfaces of bone.[738] Wilson's method (1933) was approved.[759]

3. Osteotomy. Of limited value, this may be used to correct an awkward deformity of hip or wrist.[738] Briggs described a flange osteotomy to correct deformity of the knee.

4. Arthroplasty. Different methods were described.[16, 759] Some confined its use to cases of bilateral ankylosis of hips.[738]

5. Arthrodesis. This is applied chiefly to midtarsal, subastragaloid, knee and wrist joints to convert an unstable fibrous ankylosis into a stable bony one. Other joints generally ankylose themselves.[738, 759]

6. Arthrotomy and lavage. Fisher [317] considered this valuable in subacute atrophic arthritis; he often noted a most gratifying amelioration of symptoms, sometimes complete remissions for as long as 12 to 14 years. It was approved by Savage who injected Dakin's solution, and by Broomhead who reduced chronic effusions by injecting formalin and glycerin ("Murphy's fluid") which promotes absorption by its irritant effect.

7. Synovectomy. This may be valuable in certain cases [317] but its use in atrophic arthritis is limited.[160, 759] In the type in which proliferation is confined to the synovia "it is reasonable to expect the greatest benefit from synovectomy" (Swett). But synovectomy is useless if proliferation has

progressed to the extent of severe cartilaginous ulceration and absorption, as shown in roentgenograms by a material reduction in the joint space. Inge performed synovectomy in 26 knees affected by atrophic arthritis. The response was poor. Improvement was symptomatic in 61 per cent, but functional in only 34 per cent. The rest either had recurrences or were "made worse by the operation."

8. Bone puncture or drilling; forage. This procedure (Mackenzie, 1931) was done by Kersley *under local anesthesia* in 11 cases: in five "immediate local improvement" occurred which was maintained in four. One patient who was improving before operation had general improvement. The local improvement probably resulted from the enforced rest rather than the bone drilling, as comparable results were obtained by temporary immobilization in plaster alone. [Mackenzie did his operations under general anesthesia: this may account for his better results which may have represented a nonspecific postoperative effect.—Ed.] Apparently unaware of the work of Noble Smith (1890), of Mackenzie (1931 et seq.) or of Graber-Duvernay (1932 et seq.), Hipps reported bone drilling for "acute infectious arthritis" as a "new procedure." Sixteen cases of "acute monarticular inflammation" were treated: results were "excellent" in seven, good in two, fair in four, poor in three. Smears and cultures were made of the serosanguineous exudate exuding from the bone drills: streptococci, generally nonhemolytic, occasionally hemolytic, were recovered in seven cases. It was suggested that acute arthritis starts as a primary osteitis of epiphyseal bone.

[Case histories were not given.—Ed.]

Psychotherapy. Kindersley commented on the marked cheerfulness of arthritic patients: "It seems to be a provision of Providence that this faculty is strengthened." However, these patients need frequent sympathetic discussions that they may be helped to face their future aright, and their physicians must practice simple but sound psychotherapy.[686] Much can be done by the physician who is also a friend, expressing a real human interest in the patient as a person.[40] When these patients develop a vital faith and a philosophy of living "fear goes, improved health follows, and most important of all for the future welfare of the patient, personality changes take place" (Swaim and Harris).

Prognosis; End Results. Since the viscera or vital organs rarely become affected the disease rarely shortens life though it may deprive the patient of much that lends value to life.[212] As to the prognosis in "typical rheumatoid arthritis" Stone was very pessimistic. "About one patient in ten has spontaneous remissions, to be followed sooner or later by exacerbation; spontaneous arrest may occur at any stage, but it is very uncommon before irreparable damage has been done." According to others, however, the disease frequently becomes "arrested" or "cured." The results of a composite program of treatment in one series of cases (Thompson, Wyatt, Hicks) were as follows: of 273 patients treated for 4.5 to 8 months, on discharge 24 per cent showed little or no improvement, 34 per cent were mode-

rately improved and 42 per cent were markedly improved. One to six years later, follow-up reports on 87 of the 210 benefited patients were made: nine were worse, 18 were the same as on discharge, 30 were better, 28 were well and two were dead; in other words nearly all continued to improve after discharge. Death occasionally occurs, seldom during the acute stage but from gradual " failure," in conjunction with acute depression and progressive anemia (Copeman).

Still's Disease: Still's, Chauffard's, or Felty's Syndrome

Clinical Data. In two instructive papers Portis and Schlesinger reviewed the clinical and pathologic features of this disease. These include a chronic polyarthritis which may begin acutely or insidiously. In milder cases it affects chiefly periarticular tissues but in more severe cases, like chronic progressive atrophic arthritis, it affects intra-articular tissues. Periods of septic or of mild intermittent fever, enlargement of lymph nodes, generally of spleen, and frequently of liver also, occasionally pleurisy, pericarditis and subcutaneous nodules, anemia, leukocytosis in the early stages and later sometimes leukopenia with relative lymphocytosis occur. According to Findlay [309] Still's disease is not a special type of atrophic arthritis confined to childhood; exactly the same picture occurs at all ages. Several new cases were described in detail: two fatal juvenile cases with necropsy data (Portis), one fatal juvenile case in which the patient had been under observation for six years,[167] two fatal cases of adults (Taussig), and one nonfatal case of an adult, " the first case of Still's disease reported from Australia " (Lambie).

Pathology. In only about 20 cases have necropsy data been reported. These were reviewed (Portis) and included lymphadenitis with hyperplasia of reticulum cells, splenic hyperplasia, passive hyperemia and fatty degeneration of liver, fibrinous adhesions of pericardium, of pleura and occasionally of peritoneum, cardiac enlargement without valvulitis or Aschoff bodies and articular changes presenting " the usual appearance of chronic proliferative arthritis at various stages " (fusiform swellings, contractures, effusions rarely, cellular infiltration of synovia, some formation of pannus, destruction of cartilage). Any joint may be affected. Portis emphasized the relative frequency of amyloidosis in spleen, liver or kidneys in his and other cases. His two patients had generalized amyloidosis and died of uremia as did some others mentioned in the literature. Other causes of death have been terminal colitis or pneumonia, melena, petechial hemorrhages and abdominal or subarachnoid hemorrhages. In one case [167] death resulted from hemolytic streptococcal mastoiditis, septic arthritis and septicemia. Necropsy revealed septic arthritis implanted on " obvious rheumatoid arthritis," and amyloidosis of spleen, liver, kidneys and adrenals.

[This patient was seen by one of us, W. B., and the case is the third case of rheumatoid arthritis in which joints previously affected became septic as a result of a complicating septicemia.—Ed.]

Laboratory Data. Diplococci of uncertain significance were recovered from synovial fluid in two of Schlesinger's cases. In Taussig's two fatal cases of adults hyperglobulinemia with extremely high euglobulin percentages was present. In the two cases values for total serum protein were 7.25 to 14.1 and 7.1 to 9 gm. per cent (normal 6 to 8 gm. per cent), serum albumin 1.4 to 2.4 and 2.1 to 3.9 (normal 4 to 5), serum globulin 5.6 to 11.7 and 4.3 to 5.8 (normal 1.4 to 3), euglobulin 1.7 to 3.7 and 0.8 to 2.3, pseudoglobulin 3.9 to 4.7 and 2.2 to 3.9.

Roentgenographic changes in joints differ somewhat from those of other forms of atrophic arthritis, according to Schlesinger who believed that they "could almost be described as pathognomonic of the disease." They included general decalcification, destruction of cartilage, diaphyseal overgrowth, premature ossification—"changes partly characteristic of rheumatoid arthritis and partly of osteoarthritis." A similar combination of changes was noted in Lambie's case.

Relationship to Atrophic Arthritis. Most English and American writers regard Still's disease as merely a variety of atrophic arthritis. The reactions in spleen, lymph nodes and heart suggested to Lambie that "in Still's disease the organisms supposedly responsible for the condition more frequently enter the blood and tissues than in the common forms of chronic rheumatoid arthritis." But in his case the blood was consistently sterile. Schlesinger regarded Still's disease as a "special clinical type of rheumatoid arthritis" which, for the sake of study at present, should be distinguished from the ordinary forms. [This is our viewpoint.—Ed.] Portis favored the French view that it is a special entity. Taussig recalled that manifestations of lupus erythematosus are prolonged fever, arthritis, pleurisy, pericarditis, pneumonitis, nephritis and leukopenia; cerebral lesions may occur and later hyperglobulinemia. He suggested that cases of lupus erythematosus disseminata without cutaneous reactions may not be uncommon and that lupus erythematosus disseminata, Libman-Sack's type of endocarditis, and the Still-Chauffard's and Felty's syndromes may all be manifestations of the same disorder.

Treatment. Remedies recommended were general hygienic measures, physical therapy, reactions to foreign protein and orthopedic measures as for atrophic arthritis. Gold salts, successfully used by Copeman [4] in two cases, were not recommended by Schlesinger because severe toxic reactions frequently affected his juvenile patients so treated. The use of transfusions, liver extract, supplementary vitamins and other remedies proved valueless in one case.[167]

Prognosis. This varies notably. In some apparently hopeless cases "remarkable recoveries" occur. The active stage of the disease generally lasts about five years; the infection usually subsides with the onset of puberty. Among infants the disease may prove fatal.[834]

Hypertrophic Arthritis

"Hypertrophic arthritis" is not a disease but a type of cartilaginous degeneration and osseous reaction to several different agents: trauma, gouty deposits, certain infections and unknown factors. The commonest form is "primary hypertrophic arthritis" which affects most elderly persons more or less spontaneously and usually involves several, but not many, joints. "Secondary hypertrophic arthritis" may affect persons of any age, and usually involves only one or a very few joints affected by acute trauma, an old infectious arthritis, chronic occupational trauma or the trauma resulting from a developmental defect of a joint. Thus the presence of osteophytes does not always indicate the presence of primary hypertrophic arthritis.[763]

Primary Hypertrophic (Senescent, Degenerative, Osteo-) Arthritis

Clinical Data. Patients with primary hypertrophic arthritis * react to meteorologic factors differently from those with atrophic arthritis. According to Coste and Forestier they are made worse by cold but not by dampness. In contrast to patients with atrophic arthritis, they do not feel worse at the seaside, but they too are better in dry or damp heat. Shoulder joints are affected less often by hypertrophic arthritis (in 6.6 per cent of cases) than by atrophic arthritis (in 9 per cent of cases), and less severely, according to Kuhns. Severe contractures and stiffening of shoulder joints necessitating operative procedures almost never occur in hypertrophic arthritis.

Gelatinous "synovial cysts" or "synovial lesions" develop in a few cases of Heberden's nodes over the dorsum of the fingers either between the nail and terminal phalangeal joints or between the latter and midphalangeal joints.[3] Similar lesions may affect persons without Heberden's nodes. Pathologic reactions in these nodes were described by Weber and Freudenthal. In the early stage rarefaction of connective tissue fibrils was seen without inflammation or formation of tumors. Later small oval cysts appeared which were lined with one to three rows of endothelial cells, filled with faintly staining fine granular masses forming a network. Older and larger cysts showed further diminution of connective tissue bundles, the space being occupied by star-shaped cells and fine fibrillary masses, the whole somewhat resembling the microscopic picture of Wharton's jelly in the umbilical cord. The nodules are sometimes painless, at other times quite painful.

[In the discussion of this report several methods of "curing" these lesions were noted: galvanocauterization, excision, incision and carbolization, cauterization with carbolic acid, and knocking or squashing them with a hammer. Radium was used unsuccessfully. In our experience many of these lesions need no special treatment as they are painless. Sometimes they recede or rupture and collapse spontaneously; occasionally they reform.—Ed.]

* In this section "hypertrophic arthritis" refers to the primary form.

Physicians concerned with Heberden's nodes may be interested in a historical sketch of the Heberden father and son (Hale-White).

Hypertrophic arthritis of the neck will be considered in the section on hypertrophic spondylitis.

Roentgenograms. The roentgenographic features of hypertrophic arthritis were again described.[154, 982] Attention was called to the frequent presence of small "periarticular ossicles," distinctive from osteophytes, deposited in the substance of joint capsules in fingers affected with this disease (Calthrop).

Osteophytes which affect the distal phalanges are called Heberden's nodes; those which affect the proximal phalanges are called Bouchard's nodes, according to Van Dam who believed that their structures can be explained to a great extent by studying the normal structure of the skeleton. The phalanges and metacarpals have only one epiphysis, that of the former at the proximal, that of the latter at the distal end (except in the thumb, where the metacarpal epiphysis is situated at the proximal end). The bases of the phalanges are thus epiphyseal and ossified in cartilage, and the heads [are] diaphyseal and ossified from the periosteum. The marginal zone of compact bone is sharply defined at the base, but at the head merges gradually into the spongiosa. The osseous basis of Heberden's and Bouchard's nodes consists of a composite structure, a large periosteal osteophyte connected with the periosteal head of the phalanx and a pointed cartilaginous osteophyte connected with the cartilaginous base of the next phalanx.

In cases of hypertrophic arthritis terminal and proximal interphalangeal joints commonly are affected, but the metacarpophalangeal joints rarely are affected. Curiously, the base of the thumb is not uncommonly involved. In many cases the part of the greater multangular bone lying between the bases of the first and second metacarpals is disorganized and destroyed. According to Van Dam the presence of the radial artery which loops directly over this bone may be somehow responsible.

Pathology. The articular pathology of hypertrophic arthritis was reviewed (Ghormley). "Osteo-arthritis of the same types seen by every radiologist to-day" affected the bones of a mastodon of the Post-Pleistocene Age recently found near Charleston, N. C. (Chamberlain and Taft).

Laboratory Data. Studying Cooke-Arneth counts, Gibson noted significant and essentially similar shifts to the left in both atrophic and hypertrophic arthritis as compared with normals. Collins noted such shifts to the left in cases of osteo-arthritic hips with large cyst-like areas of rarefaction in articular bone. In such cases sedimentation rates, which are generally normal in osteo-arthritis, were found to be elevated. The altered rates and shifts to the left do not permit one to assume that the disease is infective in nature. The cysts were degenerative, rather than inflammatory in origin and "are not of the osteoclastomatous nature of some other bone cysts. . . . It is now clear that true osteoarthritis of the hip is quite distinct from the simple 'osteophytosis' around joints or spine, to which the term osteo-arthritis should never be applied; the Arneth count may continue to prove of value in their differentiation. Experience with the Arneth count in this

disease also suggests that the count may be influenced by a local bone pathology which is quite independent of the general condition of the patient as reflected in the sedimentation rate."

Etiology. 1. Factor of trauma. Intricate experiments have been made to find out whether hypertrophic arthritis is a disease of usage or not. According to Van Dam, "Nature has carried out a convincing and decisive experiment on the carpo-metacarpal joints. For the carpo-metacarpal joint of the thumb is the only one of these joints which is properly mobile and at the same time the only carpo-metacarpal joint to be attacked fairly frequently by hypertrophic arthritis."

[Neither this point nor others previously noted in these Reviews have afforded convincing proof that trauma is the sole cause of primary hypertrophic arthritis. Nevertheless it is an important, perhaps the most important, predisposing and precipitating factor.—Ed.]

2. Factor of senility of articular tissues. Finn accepted the idea that the condition results from senility of cartilage: "It is a disease only if it starts early in life. . . . If we have inherited inferior cells our cartilages may give in earlier. But it seems that it is the result of the sclerosis of the blood vessels as shown in Heberden's nodes, found round the terminal joints of the fingers."

[No new data to support this idea were given.—Ed.]

3. Factor of impaired circulation. Pemberton and Scull again summarized the evidence (given in previous Reviews) which indicates that defective circulation to joints may be an important factor in the etiology of hypertrophic, as well as of atrophic, arthritis. Capillary observations made in 31 cases of symptomatic hypertrophic arthritis showed circulatory stasis in 35 per cent, intermittent flow in 32 per cent, narrowed capillaries in 75 per cent, slowed rate of flow in 28 per cent. The abnormalities were similar to, but less frequent than those seen in atrophic arthritis.

[Regardless of their importance as predisposing or aggravating factors the fact that these abnormalities are inconstantly present indicates that they cannot be the chief cause of the disease.—Ed.]

4. Factor of endocrine dysfunction. Some [281] consider the disease "endocrinal in origin" despite the fact that no known endocrine dysfunction is consistently present. Metabolic rates were above normal in 12 per cent of 116 cases, normal in 63 per cent, below normal in 25 per cent (Rawls, Ressa, Gruskin and Gordon). In this connection the work of the Silbergs is of interest. The use of anterior pituitary implants and of acid extracts of anterior lobes of pituitary glands of cattle produced hypertrophic and degenerative changes in articular cartilages of immature guinea pigs; but the changes were "similar to those reported in human acromegaly" rather than to human hypertrophic arthritis.

5. Factor of altered metabolism. Food allergy was considered by Pottenger to be an etiologic factor in hypertrophic, as well as in atrophic ar-

thritis. Sherwood entertained the idea that a vitamin C deficiency might aggravate hypertrophic (or atrophic) arthritis by increasing the interstitial fluid. Concentrations of vitamin C in the blood of 10 of his patients with hypertrophic arthritis varied considerably: 0.35 to 0.82 (av. 0.57) mg. per cent in five "county cases;" 0.48 to 1.6 (av. 1.0) mg. per cent in five "private cases"; average for the 10 cases was 0.76 mg. per cent. This average was considered normal by Rinehart and his colleagues who reported that "in a small series of cases of hypertrophic arthritis the plasma values [for vitamin C] were almost uniformly high."

6. Factor of infection. Polak echoed the conclusion of most workers that the disease is "certainly not of infectious origin." Nevertheless in its course definite inflammatory reactions may occur. Contrary to most investigators Hartung stated his belief that infection may incite symptoms: "While osteoarthritis is fundamentally a degenerative disease, there is little question that infection does play a part in precipitating pain."

[This idea has been supported by others also, but has not been proved.—Ed.]

Treatment. The great importance of reassurance was recognized. When a patient has been told that he does not have a seriously crippling or ankylosing form of arthritis "he will go home greatly improved because you have dispelled his fears" (White).[1029] In most cases rest and reduction of trauma, including that of obesity, are of first importance. Moore [676] considered the pain frequently owing to capsular stiffness, and advised patients with early osteoarthritis of hips to "keep the joint moving." He believed that despite the pain and discomfort which exercises may induce at first, increased mobility and decreased pain eventually result. [Rest has been more valuable than the deliberate use of exercises in our experience.—Ed.] The diet required is usually one with moderate caloric restrictions, especially in obese patients.[135] Pottenger sought to have patients avoid foods to which they were presumably allergic. The use of synthetic vitamin C seemed worth while to Sherwood. Massive doses of vitamin D were valueless (Steinberg). "It is quite useless to administer gold salts in osteo-arthritis." [253] Most writers [531, 583, 717, 1029] agreed that the removal of infected foci will not benefit joints in this disease, but may be indicated in certain cases to improve the patient's general health. However, the removal of foci seemed of importance to Hartung who believed that infection may precipitate pain. Kersley claimed to have noted improvement in some cases in which vaccines were used "in spite of the absence of rationale." Others considered vaccines valueless.[422]

Injections of chaulmoogra oil were given by Smith, Blocker and Tumen in 17 cases of hypertrophic arthritis: Improvement was absent in 64 per cent, "slight" in 30 per cent, "moderate" in only 6 per cent and "marked" in none. Some regarded the use of gonadotropic and thyrotropic hormones beneficial (no results given).[422] Others [791] stated that about 41 per cent of patients with mixed arthritis and osteoarthritis, especially those who were obese, "improved" following use of thyroid extract.

[One of us, F. C. H.,[404] has approved the experimental use of estrogenic hormones in cases of hypertrophic arthritis with menopausal symptoms. But most of us consider that endocrine therapy has not yet been proved to be of value in this disease. The effect of thyroid extract is chiefly, if not wholly, a weight-reducing one.—Ed.]

Roentgen therapy to provide relief of pain was approved (no results given) (Broomhead). Fever therapy also was not recommended.[885] Mecholyl iontophoresis seemed useful to some,[114] but it was considered inferior to the use of conversive heat by Licht who used six different types of physical therapy for 68 patients with osteo-arthritis. "Relief" was afforded to 25 per cent, "improvement" to 35 per cent, no benefit to 40 per cent. The beneficial effects of various forms of hydrotherapy were stressed.[211, 683, 954] Thomson favored the use of warm immersion baths with hot undercurrent douches or local hot packs to relieve pain and muscle spasms in early cases, massage with douches or hot packs in more chronic cases. Brine baths were recommended by Neligan, Fango treatments by others.[993] Currence considered his results with underwater treatment very satisfactory, "occasionally spectacular."

In some cases Tarsey obtained significant relief of pain by peri-articular and intra-articular injections of 1 per cent procaine hydrochloride. A curious method of treatment was used by Woolf in cases of hypertrophic arthritis of knees and "intractable pain." The method consisted of injection into the affected knee joint of the patient's own fat, excised from the thigh or abdominal wall, then liquefied and converted into oil to act as an articular lubricant. Thirty injections were given to 24 patients: 16 injections were called "successes," 7 were "failures," 3 were of doubtful value, 4 produced immediate relief of pain but the patients were lost sight of. No attempt was made to explain the results. Hips were found to be unsuitable for this therapy. The disadvantages of the method were recognized by Woolf who reserved it for use only in cases quite unrelieved by the usual remedies.

Orthopedic manipulation of certain osteo-arthritic joints under anesthesia was approved by some,[124, 676, 759] but considered valueless, at times harmful, by others.[738, 954] In this disease bits of cartilage or bone may become detached and form "joint mice": If they produce pain or instability they may require removal, but under other circumstances cheilotomy or the removal of chondro-osseous overgrowths has given disappointing results (Broomhead; Osgood). Platt stated that despite the technical simplicity of bone puncture or forage (drilling of the femoral head) the operation "has failed to become popular in the orthopaedic clinics of Great Britain and the United States. It would seem to be an empirical procedure and likely to be of transitory value only." [No results were reported.—Ed.] Subtrochanteric osteotomy and acetabuloplasty are reputedly indicated in selected cases (Platt). But arthrodesis of painful hips was considered by Osgood to be useful in more cases than reconstruction operations. Watson-Jones considered the use of a Smith-Petersen nail of value in performing arthrodesis. Since the synovial

changes that occur in this disease are relatively unimportant secondary effects, Swett considered synovectomy in general inappropriate. Inge also considered it theoretically contraindicated but he performed it on 20 "painful and disorganized" knees of 13 patients: 70 per cent were "improved anatomically," 90 per cent were "improved symptomatically," 60 per cent were "improved functionally. . . . Some of the most satisfactory and even dramatic results were seen in elderly patients with osteo-arthritis, several of whom were released from bed or wheel chair and restored to relatively active lives."

Secondary Hypertrophic Arthritis

In most cases of tarsometatarsophalangeal exostoses there is a definite history of trauma from blows or strains or from the continual pressure of ill-fitting footwear. Moore and Ashby accepted the theory that the actual provocative factor causes a rupture either of the periosteum, as it enters its point of insertion, or of its tendinous insertion. In the later stages of hallux valgus or hallux rigidus the compensatory changes of traumatic osteo-arthritis (secondary hypertrophic arthritis) appear. Much can be accomplished by conservative measures: padding, strapping and the use of proper shoes, graded exercises for flat feet and weak muscles. Surgical correction of bunions and excision of exostoses is often required and gives relief.[250, 678]

Backache and Sciatica

General Remarks on the Causes of Backache and Sciatica. Many short general articles on this topic appeared which described the multiple causes of backache and sciatica, the need for a detailed and rather specialized history and physical examination in every case, the use of the various physical tests and maneuvers, and roentgenologic examinations which should be made.[113, 138, 153, 286, 476, 493, 494, 685, 821] Despite the real contributions recently made to this subject it is still a very confusing one. Several classifications of the causes of backache and sciatica were presented,[113, 271, 286, 509, 742] but it is difficult after reviewing current literature to form an opinion on the relative frequency of the various causes of backache. According to Epstein 90 per cent of low back pain is due to postural defects; according to Wildman 75 per cent of backaches of men and 50 per cent of those of women are due respectively to genito-urinary and gynecologic conditions. But Raddin concluded that retroflexed and retroverted uteri rarely cause backache. According to Bankart the commonest cause of persistent low back pain is sacro-iliac strain. The commonest cause of sciatica was stated to be spinal osteo-arthritis by Echols, chronic fatigue of leg and lumbar muscles by Lindstedt, "rheumatism" by Slot, and ruptured intervertebral disk by Jaeger. In contrast several writers (Love, Adson and Craig; Poppen) considered the last to be the cause of only a small percentage of cases of sciatica. This confusion as to the relative importance of the various lesions that may produce

backache and sciatica could and should be cleared away by the coördinated efforts of several specialists. It would simplify the problem for the general practitioner, who is inclined to believe that too many specialists (urologic, gynecologic, orthopedic) jump to the conclusion that almost every backache pertains to his particular specialty.[286] [But no two or more specialists will ever agree on the cause of a backache.—Ed.] Of 417 cases of low back pain encountered by Steindler atrophic or hypertrophic arthritis was assigned to be the cause in 142, "posterior ligamentous syndrome" in 114, "myofascial syndrome" in 104, and anomalies of lumbar vertebrae in 57 cases. Steindler described a test made by injecting procaine hydrochloride to determine in a given case whether root pain is due to reflex or to compression of the root.

Backache from Urologic Lesions. Many low backaches are due, according to Wesson, to referred pain from prostatitis, to myofascitis or arthritis secondary to prostatitis which is more often nonspecific than gonococcal. He recommended urologic examinations in cases of low back pain unrelieved after a few days of conservative medical and orthopedic care.

"Suprarenal backache" noted by Hoffeld, was presumably characterized by pain over the renal region or higher, generalized weakness, fatigue and sometimes by a low sodium chloride content of blood. In one case backache was provoked by feeding foods rich in potassium.

[This report is not convincing. No pathologic or biochemical data were given. —Ed.]

Backache from Gynecologic Lesions. Backache from cervicitis was described (Raddin). Features were sacral pain with "distress" in either or both lower abdominal quadrants, extension of pain down the front or back of legs, and vaginal discharge. Pain is relieved when the patient lies down, is worse when the patient is ambulatory, and is markedly aggravated by stooping, straining at the stool, or lifting.

Backache from Gastrointestinal Disease. A few cases of backache apparently definitely caused by peptic, duodenal or jejunal ulcers were described (Compere, Jones,[501] Mixter). In four of Mixter's seven cases of middorsal backache caused by duodenal ulcer (one of which was in himself) gastrointestinal symptoms were long absent. Visceral disease (bronchiectasis was also mentioned) may cause backache, but examples were cited in which spinal lesions (fractures, extradural cysts, giant-cell tumor, tuberculosis) induced abdominal pain, sometimes simulating appendicitis.[206]

Postural Backache. This is a common,[118] some say [286] the most common, type of backache and is related to poor posture, flat feet, scoliosis, round shoulders, large abdomen, knock knees and other conditions which shift the body's center of gravity and provoke strain in the lumbar muscles and those used in walking. It is sometimes related to the use of high-heeled or ill-fitting shoes.[742] The low back pain may be associated with sciatica [579] and is usually "static," relieved by rest and recumbency, aggravated by activity and worse at the end of the day. The sequence of events includes muscle weakness, imbalance and contracture. These are evidenced by an increased

lumbar curve, pelvic asymmetry, slight adduction and internal rotation of an affected hip, tension on gluteal muscles, abductors of the hip, the piriformis and on fascia lata of the gluteus maximus. Tension on the sciatic nerve is thus produced (Lenhart and Kendall). Postural sciatica, according to Lindstedt, does not result from local mechanical conditions alone but from the operation of them in persons with a " constitutional neurosis " or general hypersensitivity to pain. The condition is treated by heat, postural exercises, swimming, reduction of weight in obese cases, the part-time use of corset or other support for the back, a ¼ to ⅞ inch lift to the heel of the shoe on the unaffected leg to shift the pelvis and abduct the affected hip, and other shoe corrections to rotate the leg externally.

Backache from " Functional Decompensation." Functional decompensation of the back was again [5] defined by Hauser as an imbalance between the capacity of the back and the load of work demanded of it. It may be part of a general condition of weakness and fatigue, and results in inflammation at the lumbosacral and sacro-iliac joints. Present are low back pain, increased spinal curves, general and local fatigue. Treatment includes rest in bed or adhesive strapping, exercise to increase the muscular capacity of the back, and if necessary, the correction of postural deformities by application of a cast.

[This condition seems vague. Its symptoms and signs simulate those of more established conditions. Is it not merely a form of postural backache or chronic lumbosacral strain?—Ed.]

" Lumbosacral and Sacro-Iliac Backache or Strain." This is a poorly defined syndrome because it undoubtedly represents not one but many different conditions. Sacro-iliac or lumbosacral backaches may arise insidiously or appear suddenly as when a person stoops to lift something, gets a sudden severe pain in the back and thereafter can rise or move only with the greatest pain and difficulty. This generally is called " lumbosacral or sacro-iliac strain " but there is no agreement on what lesion or lesions are actually responsible for the disability. Some consider a true strain or sprain responsible, microscopic tears in muscles or ligaments near the joints (Bankart, Pusitz); others blame the condition on a slight subluxation of the sacro-iliac joint (Ryan). There is no such thing as " sacro-iliac strain " according to Forrester who conceived the lesion to be a tear or stretching of soft tissues, muscles or tendons, and not a lesion of the joint itself. Some writers regard the pain as due to a " fasciitis " or " spinal fibrositis." The signs of fascial contracture were listed by Kendrick as stiffness in the lower part of the back and limitation in flexion when the knee is held extended, a positive Ober's sign, and a positive Ely's sign. Gratz concluded that the fascial planes of the human body function like joints. As a result of trauma and inflammation, fascial adhesions and " myosynovitis " involve these planes. These may produce chronic radicular muscular pain. Incident to some sudden motion these fascial adhesions may tear and produce acute

symptoms. Gratz made " pneumofasciograms " by injecting air into fascial planes; the air was distributed evenly in normals, unevenly in many arthritics and in many patients with low backache. Others believed that the use of the term " fasciitis " to explain these cases of chronic or acute low backache may not be correct since the examination of removed fascia has failed to reveal any abnormality (Harbin).

As a background for his study of " sacro-iliac joint pain " Gray made a detailed study of the finer anatomy of the sacro-iliac joints. Detailed measurements were made of the size and position of the joints and related bones; new observations, some at variance with those commonly reported, were made on pelvic inclination, mobility and axes of rotation. As a result of clinical studies Gray concluded that in cases of acute and chronic sacro-iliac pain lumbar and sacral joints are " not subluxated nor slipped but rather roughened by infection and impacted or locked at one extreme of the normal slight but real motion." In some cases of unilateral sacro-iliac pain the disease is in the lumbosacral, not the sacro-iliac joint according to Goodwyn. Straight leg raising is limited in sacro-iliac, but not in lumbosacral, lesions; flexion of lumbar portion of the spine is limited in lumbosacral, but not in sacro-iliac disease (Breck). In cases of arthritis both regions can be affected.

The treatment recommended for " lumbosacral and sacro-iliac strain or backache " was similar. For acute sacro-iliac strain Barry used injections of procaine hydrochloride to relieve acute muscle spasm; then a plaster cast for 10 days, in order that the patient may work, then a sacro-iliac belt. For both lumbosacral and sacro-iliac strain Breck advised in acute cases complete rest on a hard bed, the use of a lumbar pad, heat, strapping or a belt; casts were rarely necessary but in severe cases traction was used. For chronic cases he advised limited activity, heat, the removal of infected foci, the use of a belt, epidural injections, roentgen therapy, manipulations occasionally and if necessary a fusion operation. Gratz stated that insufflation of air may free fascial adhesions in some of these cases. Results from this treatment were satisfactory in 23 of 45 cases. According to Littlejohn rest can be overdone and in recent cases he prescribed exercises, manipulation without use of anesthesia, but if necessary with anesthesia, and fusion if no relief was noted otherwise. For sacro-iliac strain manipulation was recommended strongly by others also.[47, 363, 384, 507, 508, 528, 783, 820]

The strongest argument on behalf of manipulation was made by Gray who quoted Sir Robert Jones (1931) thus: " Forcible manipulation is a branch of surgery that from time immemorial has been neglected by our profession, and, as a direct consequence, much of it has fallen into the hands of the unqualified practitioner. Let there be no mistake; this has seriously undermined the public confidence, which has on occasion amounted to open hostility. If we honestly face the facts, this attitude should cause us no surprise. No excuse will avail us when a stiff joint which has been treated for many months by various surgeons and practitioners without effect, rapidly regains its mobility and function at the hands of an irregular practitioner. We should be self-critical, and ask why we missed such an opportunity ourselves. The problem is not

solved by pointing out mistakes made by the unqualified—the question at issue is their success. Reputations are not made in any walk of life simply by failures. Failures are common to us all, and it is a far wiser and more dignified attitude on our part to improve our armamentarium than dwell upon the mistakes made by others." Gray also quoted Paget (1867): "Learn then to imitate what is good and avoid what is bad in the practice of bone-setters." Gray described with photographs methods of manipulation, some to be used without, others with anesthesia, the former being considered safer. Mennel's methods (1938) were used by Pusitz.

Using manipulative methods without anesthesia Joster obtained "gratifying recovery" in a high percentage of cases of acute and chronic low back sprain, fasciitis, postural backache and apophyseal dislocation. Gilcreest described the manipulative methods (used with and without anesthesia) whereby he obtained "rapid and permanent cures" in most cases of lumbosacral and sacro-iliac strain. Bankart considered manipulation under anesthesia effective in 90 per cent of cases of sacro-iliac strain: arthrodesis will cure the rest. But for cases of lumbosacral strain he considered manipulation, supports and exercises of no value. According to him ligaments cannot be stretched but can be divided surgically: results therefrom were "entirely satisfactory" in almost every case. But a strong note of warning was sounded by Selig who reported a case of paraplegia from a hemorrhage following manipulation for sciatica; recovery was slow and incomplete. In many cases of low back pain and sciatica the indications for certain forms of treatment are often not clear; this is particularly true of manipulation which Selig regarded as drastic, hazardous and unjustified by the present state of our knowledge.

Backache from Tight Fascia Lata and Iliotibial Band. Ober again discussed his conception that in certain cases sacro-iliac pain and sciatica arise from contracted fasciae of the thigh and spastic iliotibial bands. He again recommended fasciotomy for selected cases as a procedure which will relieve 75 per cent of patients treated. The operation was considered useful by Barry. It was used by Smith [878] in cases of low back pain with, but not in those without, sciatica, by Pusitz only in cases in which abduction contracture was present and then only as an adjunct to other methods. Harbin also used it despite the fact that examinations of presumably affected fascia revealed no pathologic change.

Relation of the Piriformis Muscle to Sacro-Iliac Backache and Sciatica. The sciatic nerve usually emerges from the pelvis by passing beneath the piriformis muscle. But the muscle may split into two separate heads: the nerve also may divide within the pelvis into its tibial and common peroneal portions. Thus six anatomic relationships are possible, five of them being "abnormal." Some anatomists have reported the presence of an abnormal relationship in from 3 to 35 per cent, generally from 10 to 15 per cent of cadavers. Beaton and Anson found an abnormal relationship of the sciatic nerve to the piriformis muscle in 10 per cent of 240 specimens examined. When such an abnormality exists, sciatic pain may be produced if chronic in-

flammation of the piriformis muscle is present and spasm of the inflamed muscle compresses the nerve or its divisions passing between the heads of a divided muscle, or similar results may follow mere stretching of the nerve where it leaves the pelvis superior to the undivided muscle.

Diseases of Intervertebral Disks. Two main pathologic conditions affect intervertebral disks: (1) senile fragmentation and thinning, related perhaps to long continued trauma but not to acute trauma, and (2) ruptured disk with herniation of nucleus pulposus and other material; this generally occurs earlier in life than the first condition and is usually related to acute trauma.

1. Senile fragmentation of disk. In later life fragmentation of the cartilage plate may occur; granulation tissue may invade the disk from adjacent vertebral bodies and replace the nucleus pulposus so that the disk becomes merely fibrous tissue or even bone. As a result the vertebral bodies come closer together. In the thoracic and upper part of the lumbar regions kyphosis generally results. In the cervical and lower dorsal regions apophyseal subluxation generally occurs with distortion and constriction of intervertebral foramina, or in extreme cases with painful impingement of the tip of the articular process against the pedicle above or the lamina below. Hadley gave roentgenographic examples of these conditions. Symptoms produced are pain, tenderness, muscle spasm, limited motion, radiculitis, sometimes disturbances of reflexes, muscle atrophy and root pain which is aggravated by coughing or sneezing.[187]

2. Ruptured intervertebral disk; herniated nucleus pulposus. The clinical and laboratory features of this condition and methods for its diagnosis were again reviewed in a score of papers concerned with over 200 new cases proved at operation.[51, 67, 263, 304, 305, 323, 340, 375, 416, 491, 529, 566, 597, 598, 599, 600, 673, 687, 764, 856, 998, 1051] Particularly noteworthy were the papers of Barr, Bell and Spurling, Fincher and Walker, Poppen, and Love and Walsh.

Etiology. A history of trauma, such as that from lifting a heavy object, a fall, a twisting strain, or rarely that from lumbar puncture needle, was present in 50 per cent of the cases of Fincher and Walker, in 80 per cent of Barr's cases, in 71 per cent of the cases of Love and Walsh. Symptoms may appear rather suddenly after the injury (as they did in 32 per cent of Love and Walsh's cases, in 50 per cent of Barr's cases), or they may appear insidiously or suddenly some time after injury (as they did in 30 per cent of Barr's cases, in 39 per cent of those of Love and Walsh). No history of injury was present in 29 per cent of Love and Walsh's cases, in 20 per cent of Barr's cases, in 50 per cent of Fincher and Walker's.

Site of lesion. Almost any intervertebral disk may be involved but in most cases the lower lumbar disks are affected.[304, 305] In all of Barr's 58 cases lumbar or sacral disks were affected, the fourth lumbar disk in 50 per cent, the fifth in 35 per cent, sacral disk in 15 per cent. In the 100 cases of Love and Walsh 113 protruded disks were removed. A single disk was producing symptoms in 88 cases (6 cervical, 6 thoracic and 76 lumbar disks); in 12 cases more than one disk, generally lumbar, was

affected. Of the total protrusions 35 per cent affected the fourth lumbar, 42 per cent the fifth lumbar, 9 per cent the third lumbar disk (a total of 85 per cent); other lumbar disks and the thoracic and cervical disks were affected in less than five cases each. Among Poppen's 26 cases protrusions were at the fourth lumbar disk in 22, at the fifth lumbar disk in two, at more than one disk in two cases.

Symptoms. In Love and Walsh's cases of protrusion of cervical or thoracic disks a history of injury was often indefinite; in some cases pain was slight but neurologic signs and symptoms of extradural compression were present. In cases of protruded lumbar disks there was a history of injury at the onset of symptoms in 34 per cent, no history of injury in 27 per cent, and a history of injury some considerable time before symptoms in the rest. Symptoms were generally "constant and characteristic" and resulted from impingement of protruded disk material on one or more spinal nerve roots, generally of the cauda equina, the roots of which form the lumbosacral plexus.[51] The sex incidence was almost identical in the series of Barr (males 75 per cent, females 25 per cent) and of Love and Walsh (males 77 per cent, females 23 per cent).

In most cases the patient complains of low back pain, occasionally without, but almost always (in 92 per cent of cases) [600] associated with sciatica. Indeed sciatica is such a dominant symptom that some writers now consider the majority of cases of sciatica to be caused by ruptured disks.[491] Herniated disks were the cause in 24 of 31 consecutive cases of low back pain with sciatica in which Fincher and Walker made lipiodol studies. Others [599, 764] insist that only a small percentage of cases of sciatica are caused by ruptured disks and Barr warned of the untempered enthusiasm of those who assume that this entity is the cause of all sciatica. Nevertheless it is an important and common cause of sciatica and should be thought of in all chronic cases.

Sciatica was unilateral in 80 per cent, bilateral in 20 per cent of Barr's cases, unilateral in 77 per cent, bilateral in 23 per cent of the cases of Love and Walsh in which sciatica was present. Additional symptoms and signs included local lumbar tenderness (in 50 per cent), root pain on coughing or sneezing or on jugular compression (in 39 and 40 per cent), kyphos or flat back (90 per cent), sciatic scoliosis (60 per cent), positive Lasègue's sign or limitation of ability to raise the extended leg (in 82 and 100 per cent), ankle jerk absent or reduced (in 50 and 57 per cent), sensory changes consisting of anesthesia or hyperesthesia (in 35 and 49 per cent), motor changes consisting of muscle weakness or paralysis (in 15 and 26 per cent), sphincter disturbances (in 5 and 8 per cent): the percentages were those noted by Barr, and by Love and Walsh. In some cases neurologic signs were absent; in many cases the only signs were sciatica and reduced Achilles reflex. Symptoms were constant in 60 per cent of Barr's cases but in only 14 per cent of those of Love and Walsh; they were intermittent in 40 and 86 per cent of these cases respectively. The intermittency of symptoms probably is due to the fact that some protrusions are restored partially and temporarily and later the material extrudes again. It has been noted that

kyphotic flexion of the spine of cadavers caused a return of protruded disks into almost normal position.[600]

Diagnosis. Obviously the condition presents no classic picture; its symptoms resemble those of sacro-iliac and lumbosacral strain or of thickened ligamenta flava. Ordinary roentgenograms are of little value in diagnosis. Many persons have narrowed intervertebral spaces which are not associated with clinical signs and symptoms; in cases of ruptured disks producing pain, narrowed intervertebral spaces are not always present.[67] To make a presumptive preoperative diagnosis of ruptured disk, examination of spinal fluid and spinograms made after injection of air or lipiodol are required. Since most of the protrusions are low in the spine, spinal puncture should be as low as possible, preferably at the lumbosacral interspace [51, 764] or at the second or third lumbar interspace.[598] The value of total protein in spinal fluid was over 40 mg. per cent in about 75 per cent,[598] about 80 per cent [529] and 85 per cent [51] of cases in the series reported. In Love and Walsh's cases of cervical and thoracic protrusions it was 40 mg. in 29 per cent, more than 40 mg. in 71 per cent; in 80 per cent of their cases of lumbar protrusions it was 40 mg. or more (up to 240 mg.).

If the spinal fluid protein is more than 40 mg. per cent (or sometimes even if it is normal but severe protracted sciatica is present) [764] a spinogram should be made. Formerly lipiodol was used routinely but because lipiodol occasionally produces irritating symptoms if not removed, it is now recommended that lipiodol be used with considerable discretion.[375] Since 90 to 95 per cent of patients with sciatica recover spontaneously or on conservative treatment patients with sciatica should not be subjected routinely to a highly technical and possibly irritating lipiodol spinogram (Barr). Some preferred spinograms made by injecting air (Poppen); most defects are revealed by "pneumospinograms"; the air is innocuous and disappears rapidly. Others [599] considered the reversed Queckenstedt test useful in cases strongly suggestive of ruptured disk but in which protein in the spinal fluid is normal. When lipiodol is used most investigators injected 4 to 5 c.c.[51, 529, 600, 687, 764] Harbin used 3 c.c. According to Bell and Spurling 2 c.c. are sufficient and entirely harmless in their 10 years' experience; this amount gave them better visualization than larger amounts which were considered unnecessary and possibly harmful. But others [566, 1051] considered the use of 5 c.c. necessary; 2 c.c. may fail to reveal defects produced by slight protrusions. Mild reactions to unremoved lipiodol were occasionally noted: temporary retention of urine, slight fever and pain; hence the use of such spinograms entails a slight risk but one which is "without any real danger." [1051] Fincher and Walker noted no reactions in their 31 cases and cited the experiments of Globus (1937) in which no neurologic residues and no encysted lipiodol were seen. Lipiodol may occasionally become encysted in cases in which inflammatory conditions have preceded its use.[764] Hence lipiodol should not be used in the presence of suspected inflammatory lesions; it should never be injected at temperatures above that of the body; it should not be used if it is cloudy.[600] Spinograms were made after injection of lipiodol by Echols only in cases of sciatica unresponsive to the usual medical and orthopedic measures, by Barr only in cases of intractable or recurrent sciatica with neurologic changes owing to pressure on a nerve root, by Poppen only in suspected cases of protrusion in which spinograms after injection of air were inconclusive. The technic of making spinograms and their interpretation were described in detail.[67, 566, 1051] The filling defects produced by the ruptured disks are visible in over 90 per cent of cases according to Barr; but since normal nerve root sleeves fill with great variability the presence of an abnormal shadow of a root sleeve in a roentgenogram should not be considered too significant unless neurologic examination indicates disease at the same level.[67] Very occasional false positive defects are revealed by spinograms: in two such cases Poppen at operation found only chronic thickening of the arachnoid.

Treatment. Laminectomy and removal of the protruded disk material were successful in practically all the reported cases. Relief was obtained in all of the 24 cases of Fincher and Walker, in the four cases of Kendrick and Bunts, and in 24 of Poppen's 26 cases. Of Barr's 58 patients so treated, 54 were " well or markedly improved "; three were unimproved; there was one postoperative death. In their series of 100 cases Love and Walsh reported relief and no recurrences in 99 cases, and one postoperative death; an additional 100 laminectomies were later done without a death.[598] In Love's first series of 100 cases (Love and Walsh) there were no recurrences of pain, but in one of the next 50 surgical cases, pain returned two months after operation. A second operation was performed and complete relief was obtained without a later recurrence. At the first operation probably only part of the fragmented disk protruded; more protruded later.

The question of whether the spine should be fused at the region of laminectomy is unsettled. If articular facets were left intact Barr considered fusion unnecessary, otherwise he favored it to prevent symptoms of a weak back. Love and his colleagues preserved the facets and found fusion unnecessary in 150 cases. In many cases the protruded disks were associated with thickened ligamenta flava; these were resected.[67, 600] Jaeger noted that sometimes the cartilage was injured so far laterally that no filling defect was visible in spinograms; cartilage fragments pressed on the caudal roots, not inside the dura, but as they passed through intervertebral foramina. In such cases pain was relieved by bilateral rhizotomy of the sensory root.

Symptoms Caused by Narrowed Intervertebral Foramina. When apophyseal subluxation occurs either as a result of senile fragmentation or of traumatic rupture of intervertebral disks, intervertebral foramina are encroached on by masses of connective tissue from the posterior joint capsule and the disk margin or by bony exostoses. As a result nerve roots are crowded and sometimes actual fibrosis occurs (Hadley). Turner discussed his study (previously reported with Oppenheimer,[4, 5]) of 70 cases of narrowed cervical intervertebral spaces, with or without hypertrophic arthritis, but associated with diminished size of intervertebral foramina. Pains in the shoulder girdle, arms and precordium were commonly produced. Treatment was the use of repeated traction with the head and neck in a sling.[4]

" The Swollen Atrophic Hand." Under this title Oppenheimer described 14 cases in which unilateral narrowing of upper cervical intervertebral foramina produced swelling and atrophy of the hand on the same side. The patients complained chiefly of their hands, not of their neck. They had swelling and pain of the whole hand and wrist, a wrist alone, or of only one or two fingers. It was not confined to periarticular tissues. Redness was absent. Joints were freely movable. Sometimes there was atrophy of skin and interosseous muscles. In four of the 14 cases a degenerative reaction was present in the muscles of the affected arm. In all recurrent " rheumatic pain " in the shoulder girdle or deltoid region of the affected side, tingling sensations in finger tips, and subjective but no objective sensory disturbances

had been present for weeks or years. In some cases there were no symptoms referable to the neck. Roentgenograms revealed decalcification of the bones of the affected hands and wrists, but joint spaces were normal (unlike atrophic arthritis). Anteroposterior and lateral roentgenograms of the cervical portion of the spine did not clearly demonstrate the lesions which were shown by a special technic for oblique views of the neck. In each case there was narrowing of intervertebral foramina above or including those of the fourth cervical vertebra. Swelling and atrophy of the hand were independent of the disease producing the narrowing of the foramina. Causes of the latter were fractures of cervical vertebrae, exostosis, subluxation of vertebrae, thinning of intervertebral disks, and isolated arthritis of the cervical portion of the spine. Rarefaction of the bones of the hand occurred with swelling and atrophy of the skin but was independent of atrophy of the interosseous muscles. The condition represents a trophic disturbance caused by pressure on cervical nerve roots within the intervertebral foramina, and must be distinguished from the swellings which may accompany neuritis, scleroderma, acrodermatitis atrophicans, and atrophic arthritis.

Ultrashort wave treatments over the neck were given to seven patients: six responded almost at once, pain and swelling subsided after three or four treatments and did not recur; within several months muscles and bones became normal or almost so. No other therapy was used: decongestion of nerve sheaths may have been accomplished. The unrelieved patient refused operation, although a fractured articular process was displaced into the intervertebral foramen.

[This is an interesting report which needs verification.—Ed.]

Backache and Sciatica from Hypertrophied Ligamenta Flava. The close anatomic connection of this ligament, the cauda equina and sciatic nerve was described.[7] Presumably as the result of trauma (fall on buttocks, lifting heavy objects) in most cases (sometimes perhaps as the result of inflammation) the ligaments are stretched or partially torn (or inflamed) and heal with thickening and contracture. This produces pressure on nerve roots as they emerge from intervertebral foramina. Symptoms produced are identical with those from herniated disk; the two conditions cannot be differentiated even by spinograms. This is immaterial as the treatment of both involves laminectomy. Often both conditions coexist. Common symptoms are low back pain, chronic or intermittent, generally associated with sciatica; the Achilles reflex usually is reduced or absent. Concentration of protein in the spinal fluid is increased. Lipiodol spinograms reveal partial or complete subarachnoid block. Treatment consists of laminectomy and wide removal of the enlarged ligamentous material. Relief in 15 cases was reported (Abbott, Brown,[127] Flothow, Harbin). The average thickness of the normal ligament at the fourth lumbar space is 4.4 mm.; the diseased ligaments were from 11 to 30 mm. thick and were markedly fibrosed (Abbott).

Backache from Developmental Anomalies. Among 1000 patients with low back pain seen by Williams 29 per cent had lumbosacral anomalies, 7 per cent had sacralization, 9 per cent lumbarization, 8 per cent imperfect fusion of sacral lateral masses, 3 per cent spondylolisthesis, 2 per cent fragmentation and anomalies of facets. Williams concluded that most patients with such anomalies have localized or segmental symptoms caused by degenerative changes induced thereby, or by direct mechanical involvement of nerve roots. [Many patients with congenital spinal anomalies have no symptoms. It would have been interesting had Williams also noted the incidence of such anomalies in 1000 persons *without* low back pain.—Ed.] According to Goodwyn such anomalies may not produce pain per se but may produce pain when aggravated by injury or affected by "toxemia." Congenital anomalies of lumbar spine seemed to Clarkson and Barker to be less frequent causes of low back pain than narrowed lumbosacral joints; they reported two cases of backache owing to false articulations between large clubbed transverse processes and the sacrum. Two cases of unusual hereditary malformation of cervical and thoracic vertebrae were noted by Jarcho and Levin in a brother and sister; the condition was related to the Klippel-Feil cervical anomaly—short, rigid neck, low hair line.

Backache from Spondylolisthesis. Details of 583 cases of lumbar spondylolisthesis seen at The Mayo Clinic in 20 years were reported by Meyerding.

In 82 per cent of the cases there was a forward displacement of the fifth lumbar vertebra on the sacrum. Interlumbar displacement was present in the rest. Many persons have symptomless spondylolisthesis: the condition was noted in more than 10 per cent of clinic patients. But in all the 583 cases reviewed symptoms were present: backache in 63 per cent, backache and pain in legs in 17 per cent, pain in hips and legs in 8 per cent, deformity, stiffness, or paralysis in 2 per cent, miscellaneous symptoms in 10 per cent. The condition was previously diagnosed in only 7 per cent. The presence of the anomaly can be suspected on other grounds but roentgenologic diagnosis is best. A history of trauma was found in only 48 per cent. Men were affected in 70 per cent, women in 30 per cent of cases; among Williams' 32 cases sex incidence was about equal. Conservative treatment was used in 83 per cent of Meyerding's cases: in mild cases a lumbosacral corset; in more severe cases reduction of the deformity by traction and the prevention of its recurrence by the use of a cast. Surgical treatment (double massive bone graft) was necessary in only 17 per cent.

Reverse Spondylolisthesis; Posterior Displacement of the Fifth Lumbar Vertebra on the Sacrum. This condition was present in 4 per cent of Meyerding's cases. The condition was described by Smith (1934) who discussed it again.[878] Such a posterior displacement which has seemed theoretically impossible to many does occur; the displacement seldom exceeds ¼ inch. The fifth lumbar body rests, not on the sacrum, but on the nucleus pulposus. From this position it can tip backward easily if the lateral articulations are

so constructed as to make this possible. According to Smith, in most cases of posterior displacement the articulations are of the anteroposterior or asymmetrical type. Symptoms of reverse spondylolisthesis are repeated attacks of low back pain which may be initiated suddenly by bending; pain in thigh and leg and sciatic scoliosis may occur.

Coccydynia (Coccygodynia). For cases of acute traumatic coccydynia Pusitz recommended manipulation, with or without anesthesia, to correct displacement and prevent adhesions. Treatments are given semi-weekly, and may be temporarily painful.

Additional Comments on the Treatment of Backache and Sciatica. It becomes increasingly obvious that numerous conditions may cause low back pain and sciatica. "It is as antiquated to make a diagnosis of 'sciatica' today as it is to make a diagnosis of 'headache.'" [600] Two forms of treatment used in selected cases of a variety of conditions producing low back pain and sciatica were injections of analgesics, and fusion operations. Epidural injections of normal saline solution were used in cases of "chronic fasciitis." [528] For several conditions Steel used intraneural and epidural injections of procaine hydrochloride, and paravertebral injections of alcohol. The technic was described. Epidural injections of procaine, in conjunction with manipulations, gave successful results in 75 per cent of "some four or five hundred cases of [presumably rheumatic] sciatica" encountered by Slot. Irwig considered results from eucupine oil more lasting than those from procaine.

Indications for fusion operations in cases of low back pain and sciatica were restated.[271, 375, 670, 878] Most physicians, as did Smith,[878] recommended the use of fusion operations only in cases unrelieved by conservative measures. In about 90 per cent of Smith's cases of low back pain response was satisfactory to conservative remedies; in the rest lumbosacral fusion was used; results were good in 80 per cent of those so treated. According to Eggers fusion should *not* be reserved for "resistant cases"; in most of these, benefit will not result. Fusion was recommended chiefly for patients relieved by rest, made worse with activity, again relieved by rest. Such reactions indicate the presence of some mechanical irritation. Fusion operations were performed on the middle-aged, not on the old or the young. The number of persons whose condition is suitable for fusion operation is small and insignificant compared to the total number of persons with backache. Goodwyn's views were also conservative; he noted permanent relief in only a few cases of sacro-iliac and low back pain.

Miscellaneous Conditions of the Spine. 1. Spinal malignancy. In such cases the constancy and severity of pain rather soon become notable features; pain is not relieved by heat, rest or splints and usually requires narcotics in time. In suspected cases roentgenograms taken from different angles and made from time to time are required for diagnosis. Pain may antedate roentgenographic evidence of metastatic malignancy by two to 12 months or more. Miltner noted complete relief of pain in 41 of 57 patients treated by

subarachnoid injections of alcohol combined with roentgen therapy (as used by Poppen, 1936). In special cases plaster jackets or body braces were used.

2. Spinal actinomycosis. One case was reported (Flynn and Gillies).

3. "Neurotic backs." This is not a wholly functional condition but represents a traumatic neurosis secondary to real injury. Patients so affected are usually worried, apprehensive of their physical examination, highly nervous but coöperative, open-minded and sincere in describing their complaints. Limited motions and muscle spasms are absent; patients are inaccurate in relocating their painful spots. The latter are usually tender only on deep pressure. Physicians should gain the patient's confidence by making roentgenograms and tests to show one's earnest desire to find any trouble. It is psychologically useful to deliberate over the final diagnosis for several days or weeks. Then a careful sincere explanation of the condition by the physician may end the neurosis (Forrester).

4. Backache of malingerers. The malingerer who claims to have been injured, often enters the office with canes or on crutches long after the supposed injury. He is belligerent, uncoöperative, and objects to questioning. He feigns tenderness on the slightest pressure and either refuses to attempt certain motions (such as kicking an imaginary football) or grossly exaggerates his actions while attempting them. He exhibits many tender spots, but when they are marked with a skin pencil he cannot relocate them on subsequent examinations. When he thinks he is not being watched, he may be observed to tie his shoe laces, or pull on his trousers normally (Forrester).

Sciatica: Additional Comments. Several reports concerned the subject of "sciatica" in a general way.[118, 256, 533, 838, 875, 876, 914, 1021, 1041] Classifications of the causes of sciatic neuralgia and neuritis were attempted.[875, 1015]

Sciatic fibrositis. According to Kersley most cases of "sciatica" are due to fibrositis either directly involving the nerve trunk or causing reflex pain from "fibrositic congestion and small cob-web adhesions in gluteal and lumbar muscles and posterior sacro-iliac ligaments." Others [807, 838] agreed with this view. Symptoms of "sciatic fibrositis" were said by Robinson to include "the type of pain common to all these syndromes," tenderness in gluteus medius or maximus, without muscle atrophy or abnormal tendon reflexes. [The problem of sciatic fibrositis is a very confused one. By this term some writers have meant a fibrositis of the investing tissues of the sciatic nerve. But current writers are using the term to designate not a perineural fibrositis but a fibrositis of muscles and tendons supplied by the sciatic nerve. In either case the condition is ill-defined because of inadequate pathologic data.—Ed.] Sciatic fibrositis was treated by the usual remedies for fibrositis: physical therapy, counterirritants, rest, later massage to sacro-iliac and gluteal regions, removal of infected foci and if necessary, manipulation or epidural injections (Kersley).

Previously considered (under "Effect of jaundice on atrophic arthritis") were the five cases of "sciatic neuritis" which preceded the onset of hepatitis and in which pain was relieved with the onset of jaundice (Lichtman).

For "sciatic pain of unknown origin" Haggart used a combination of two, sometimes three procedures: (1) perineural injection of the sciatic nerve, (2) traction to the affected extremity, (3) manipulation of the lower back under anesthesia. The majority of 75 patients so treated were benefited. Slot also used epidural injections of procaine hydrochloride and manipulation under anesthesia in cases of "rheumatic sciatica." Epidural injections were approved by Winkler but considered valueless by Duncan in cases of "sciatic pain." Other remedies recommended were short-wave diathermy, roentgen therapy, sinusoidal currents (Weiss) and the usual remedies; rest in bed on a hard mattress, Buck's extension, etc.[256, 1041] Injections into the nerve were condemned. Intramuscular injections of vitamin B (betaxin) were given by Stevenson to 18 patients with "sciatica": an equal number were "cured," "very much improved" and unimproved. Bennett and Cash treated 20 cases of intractable "sciatic neuritis" by fever therapy alone or with epidural injections: marked to complete relief was noted in 80 per cent.

Spondylitis

Most writers [137, 278, 377] accepted the traditional classification of the common forms of spondylitis; atrophic or ankylosing spondylitis (spondylitis rhizomelique) and hypertrophic spondylitis (spondylitis osteo-arthritica) and stressed the usual chief differential points as noted by Gordon: In hypertrophic spondylitis there is no ankylosis however extensive and numerous the osteophytes are; in atrophic (rheumatoid) spondylitis there is no vertebral lipping; in the former osteophytes represent true bone; in the latter what appears to be new bone is simply a deposit of lime salts in ligaments.

[Until recently physicians, including roentgenologists, paid little attention to parts of the spine other than vertebral bodies, but recently orthopedists and neurosurgeons have made much progress by studying the finer relationships among the intervertebral disks, foramina, spinal cord and nerve roots. As a result several "new" spinal syndromes have been described: herniated nucleus pulposus, degenerative fragmentation of disks with apophyseal subluxation, the facet syndrome, hypertrophied ligamenta flava, etc. Despite the broadened outlook of their colleagues it seems to us that most clinicians and rheumatologists have continued to consider spondylitis only in relation to the presence of exostosis or atrophy of vertebral bodies or of ligamentous calcification, and largely have ignored lesions of the only true joints of the spine—the apophyseal joints. Exclusive of such specific diseases as tuberculosis, brucellosis or Charcot's disease of the spine there are doubtless several "nonspecific" diseases of apophyseal joints and vertebral bodies that cannot be disposed of by the simple classification of atrophic and hypertrophic spondylitis. The recent introduction of the term "spondylarthritis" to indicate disease of apophyseal joints in contrast to "spondylitis," a disease of vertebral bodies, may at first be confusing, but is distinctly a step in the right direction. Hence we have seen fit to present the following studies of Oppenheimer in some detail to serve as an introduction to some newer ideas on spinal pathology. Oppenheimer's classification probably will need much modification; the descriptions of some of his types were based on an experience with only a few (4 to 14) cases. Nevertheless his papers are stimulating and deserve attention. The

roentgenographic illustrations therein will clarify his conceptions better than we can here.—Ed.]

Oppenheimer presented a new classification based on a clinical and roentgenologic study of 147 cases. He considered it most important to distinguish between affections of the vertebral bodies (spondylitis), of the apophyseal or posterior intervertebral joints (spondylarthritis) and of the spinal ligaments (spondylosis ligamentosa). The vertebral bodies do not form true joints; the only true joints of the spine, that is those possessing a synovial membrane, are the small apophyseal joints. These may become affected by the various forms of arthritis primarily, independently, and exclusively of vertebral bodies, or, as parts of the vertebrae, may participate in localized or systemic diseases of the spine. Likewise the spinal ligaments may become affected alone (without disease of disks or apophyseal joints) as they do in Oppenheimer's type of spondylosis ossificans ligamentosa (not the same as Knagg's spondylitis ossificans ligamentosa), or the ligaments may calcify as a secondary manifestation of a variety of spinal lesions; e.g., spondylarthritis ankylopoietica, hypertrophic spondylitis, Pott's disease, and traumatic lesions. Hence Oppenheimer made the following definitions: (1) spondylitis, an inflammatory disease of the spine, especially the vertebral bodies, either rarefying, as in tuberculosis, or hypertrophic as in low-grade infections (he noted one form supposedly related to an amebic infestation) and in mechanical irritation resulting, for example, from thinning of disks; (2) spondylarthritis is an inflammation of the true spinal joints; i.e., the apophyseal intervertebral articulations; (3) spondylosis ossificans ligamentosa is an ossification of spinal ligaments which may appear with, but sometimes without, changes in vertebral bodies, intervertebral disks and apophyseal joints. "Calcification of spinal ligaments is a very common and totally uncharacteristic response to a great variety of vertebral lesions,—inflammatory, degenerative, destructive or traumatic."

[Oppenheimer seems to make no distinction between calcification and ossification. —Ed.]

1. *Spondylarthritis.* Four types of spondylarthritis were recognized: 1. Acute (atrophic) spondylarthritis (not the same as ordinary atrophic spondylitis) is a disease which is strictly localized (in five of Oppenheimer's cases to cervical, in two cases to lumbosacral spine) and represents an acute infection of certain apophyseal joints with inflammation of their synovia but the *cartilage remains intact* (the joint space does not disappear in roentgenograms). It represents a localized, usually monarticular, apophyseal arthritis with transient swelling of capsule which in Oppenheimer's cases was the aftermath of acute respiratory infection or chronic tonsillitis. [Does this represent an acute phase of the chronic type of spondylarthritis or of atrophic spondylitis?—Ed.] Since the vertebral bodies and disks are unaffected and the apophyseal cartilages remain intact, restoration of joint function is possible and occurred in several cases. "Acute atrophic spondylarthritis can be cured."

2. Chronic atrophic spondylarthritis is a type which also is not to be confused with ordinary chronic atrophic spondylitis but is a chronic *localized* disease of apophyseal joints, not of vertebral bodies or spinal ligaments; it is presumably infectious, characterized by capsular swelling, rarefaction of apophyseal bone, later irreparable destruction of apophyseal cartilage. "The distinction between acute and chronic

atrophic spondylarthritis is here not based upon the duration of the clinical symptoms, but is determined by the absence, in the former, of destruction of cartilage. Roentgenologically, therefore, the differentiation is made according to the width (normal or diminished) of the involved joint space. . . . Chronic atrophic spondylarthritis can be arrested by successful treatment of the coexistent infection."

"Atrophic spondylarthritis [the acute and chronic forms numbered 1 and 2] is independent of other systemic spinal diseases; there is especially no correlation either with spondylosis ossificans ligamentosa or with the various types of spondylitis."

3. Ankylopoietic spondylarthritis is a synonym for ordinary atrophic spondylitis, spondylitis rhizomelique, Strümpell-Marie's disease, Bechterew's disease, spondylitis ossificans ligamentosa of Knaggs. "This is a typical atrophic arthritis of the apophyseal joints (as proved histologically) with a marked tendency toward systemic involvement of all the apophyseal articulations and demineralization of the vertebral column. It is presumably an infection producing proliferative inflammation of synovial membranes, destruction of apophyseal cartilages, pronounced osteoporosis, fibrosis, later bony ankylosis of facets [this last being the criterion of the diseased] and secondary ossification of the ligamenta flava and longitudinal ligaments." Bony ankylosis produces the "bamboo spine" appearance: the vertebral bodies become rarefied, the disks (intervertebral spaces) remain normal or sometimes widen as they compress the softened vertebral bodies. As a rule the sacro-iliac joints are simultaneously involved, and the costo-transversal, hip and shoulder joints participate less commonly. The intervertebral foramina may be reduced in width to less than one-half of their original diameter by concentric calcifications. At earlier stages the swollen capsule also may compress the nerve roots. Whether or not such constriction will lead to actual compression of the nerves depends on the relation between the width of the foramina and the caliber of the nerves.

Oppenheimer stated, "It would appear justifiable perhaps to consider the three types of atrophic spondylarthritis—acute, chronic, and ankylopoietic, as phases of a single continuum without assigning to any single one or to all of them a specific cause. The pathological findings described may be the expression of reactions of these areas to stimuli of a number of kinds, but the reaction may stop at any point; or it may continue to the stage described as ankylopoietic spondylarthritis."

[We wonder whether the author's follow-up is sufficiently long to justify these statements.—Ed.]

4. Hypertrophic spondylarthritis also is an affection of apophyseal joints, not of vertebral bodies. Oppenheimer noted a "primary infectious form" in 14 cases, in 13 of which *Endamoeba histolytica* were found in the stools. The lesions were in the thoracic portion of the spine in seven, lumbar in three, cervical in four cases. Articular processes were greatly increased in density, facets were ragged, apophyseal joint spaces were irregularly narrowed, and there were thorn-shaped exostoses at the posterior borders of the contiguous facets: from two to many articulations were affected. Intervertebral spaces (disks) and vertebral bodies were normal. In three cases parts of the anterior longitudinal ligaments were calcified. Relief was obtained from anti-amebic treatment.

[Further evidence is necessary before accepting the view that amebae are responsible for this disease.—Ed.]

Another type of hypertrophic spondylarthritis was noted (a primary mechanical form) caused by mechanical irritation from traumatic or degenerative thinning of intervertebral disks and subsequent displacement of apophyseal cartilages. In apophyseal joints ulceration and degeneration of cartilage, eburnation of articular surfaces of the apophyseal joints, villous hypertrophy of the synovial membrane, hypertrophic exostoses, ossification of intra-articular ligament, then occur. Pathologic bony formations on contiguous facets may fuse, but this type of bony ankylosis is differentiated from that in ankylopoietic spondylarthritis by the absence of general rarefaction and the presence of residual exostosis.

All the forms of spondylarthritis so far described were regarded as being primary types to be distinguished from the secondary forms—diseases of *apophyseal joints* secondary to such conditions as tuberculosis, brucellosis, and osteomyelitis of *vertebral bodies*. As a matter of fact these diseases spread to apophyseal joints much more rarely than one might suppose. "It would seem that the distant position of the articular processes as well as the greater resistance of their compact bone prevents the [apophyseal] articulations from being easily affected." In osteoperiostitis, hypertrophic osteitis and Paget's disease articular processes may participate in the vertebral affection, but the apophyseal joint spaces often remain normal in width, and the outlines of the facets remain smooth. In general apophyseal cartilages remain intact unless statical alterations resulting from the disease of vertebral bodies secondarily induce degeneration of apophyseal cartilage and then hypertrophic spondylarthritis.

II. *Types of spondylitis.* Two chief types of *spondylitis* were recognized by Oppenheimer: (*a*) tuberculous spondylitis, a disease of vertebral bodies which affects apophyseal joints rarely (tuberculous spondylarthritis); (*b*) hypertrophic spondylitis, a disease characterized by exostoses at the margins of vertebral bodies, which may result, according to Oppenheimer, either from a low grade infection, or much more commonly from thinning of intervertebral disks. [We doubt that infection plays a rôle in hypertrophic spondylitis.—Ed.] In hypertrophic spondylitis, eburnation and exostoses of vertebral bodies, calcification of longitudinal ligaments and subluxation of articular processes occur. Some cases of hypertrophic spondylitis are associated with hypertrophic spondylarthritis. But only in 14 per cent of Oppenheimer's 72 cases of hypertrophic spondylitis was there also secondary hypertrophic spondylarthritis (eburnation of facets, exostoses at the articular processes of apophyseal joints).

Relationship between Hypertrophic Spondylitis and Hypertrophic Spondylarthritis. As indicated in the foregoing discussion the apophyseal joints may be affected in one way or another without similar reactions occurring in vertebral "joints" and vice versa. Hence hypertrophic spondylarthritis may occur without hypertrophic spondylitis, and hypertrophic spondylitis may (and generally does) occur without hypertrophic spondylarthritis. "This is not surprising, for the apophyseal joints differ in both structure and function from the intervertebral synchondroses formed by the disks and the adjacent vertebral surfaces. The vulnerability of the articular cartilage is variable in different persons; therefore mechanical stress does not of necessity lead in every instance to lesions of cartilage inducing arthritis. Hypertrophic spondylitis is very often the result of lesions of the disks. On the other hand thinning of the disks does not invariably lead to increased bone formation at the vertebral bodies. Similarly the abnormal stress upon the facets in this condition does not of necessity induce lesions of cartilages. It would seem that both the vulnerability of the cartilage and the readiness of the bone to respond by formation of exostoses are important factors in the pathogenesis of these conditions. This is shown by those instances in which no bone reactions develop at both the vertebral bodies and the articular processes in spite of marked thinning of the disks, contact between the bodies and pronounced thinning of the articular cartilages." In these cases none of the characteristics of hypertrophic arthritis become evident roentgenographically; only the intervertebral and the joint spaces seem to be affected; bones are not involved. But in thinning of disks, enormous exostoses may occur on the corresponding vertebral bodies without narrowing of the apophyseal joint space or change in facets. This indicates that vertebral bodies responded to the abnormal mechanical stress produced by the thinning of the disks, but cartilages resisted. "Regardless of the presence or the absence of these secondary changes, thinning of disks is the cause of their eventual development, for it leads to contact between vertebral bodies, to abnormal tension upon ligaments, to displacement of articular processes, and to narrowing of the intervertebral foramina." The type of spondylarthritis that develops under these circumstances was called the "discogenetic" form of hypertrophic spondylarthritis.

III. Spondylosis Ossificans Ligamentosa. This condition was distinguished from the secondary ligamentous ossification that is associated with several spinal diseases (notably ankylopoietic spondylarthritis) and was described by Oppenheimer as a systemic ossification of ligaments without changes of disks or apophyseal joints, usually discovered accidentally during examinations of chest in persons over 50 years of age without clinical symptoms. Apophyseal joints remain normal. Posture is not altered. Involvement was greatest in the less mobile thoracic portion of the spine, least in the more mobile cervical and lumbar regions; hence spinal mobility usually seemed intact.

Atrophic Spondylitis (Spondylitis Ankylopoietica)

Clinical Data. Most writers classified this as atrophic (rheumatoid) arthritis of the spine. Others [377, 982] concluded that it is closely related to, but not identical with, atrophic arthritis, among other reasons because the sex incidence is reversed and because of serologic differences between the two conditions. The usual clinical data were reviewed.[137, 377] Scott repeated his argument that the pain and stiffness of the lower part of the spine and sacro-iliac joints are quite late, not early signs of the disease. According to him the initial pre-spondylitic symptoms begin generally about the age of 12 to 14 years as wandering pains in limbs, joints, chest and abdomen at which time roentgenograms of sacro-iliac joints do not reveal any abnormality; perhaps two years later the pre-spondylitic symptoms "begin in earnest" with more definite pains in knees, chest, shoulders; at this time roentgenographic changes in sacro-iliac joints are already present despite which there is as yet no stiffness, backache or sacro-iliac pain. By the time sacro-iliac and low back pain begins the disease is thought by Scott to be several years old. "Pathologic changes can be detected in sacro-iliac joints about six or seven years before there are any clinical signs whatever of arthritis in the spine." Scott stated that "sacro-iliac changes" were pathognomonic of this type of spondylitis "for they have been present in all of the 300 patients under observation." If roentgenograms of sacro-iliac joints were to be made of young patients with recurrent attacks of rheumatic pains in various parts, "spondylitis adolescens" could be "recognized several years before the backache period commences." This view was not acceptable to others. Thus Gordon wrote "Scott's contention that every case shows evidence of sacral ankylosis cannot be supported by observers whose clinical experience is at all extensive."

Laboratory Data. Arneth counts were similar to those in cases of atrophic arthritis.[357] Spondylitics with elevated sedimentation rates also showed the formol-gel reaction most frequently.[360]

Etiology. Nothing definitely new on etiology was presented. The French concept that gonorrhea can cause chronic atrophic spondylitis was disputed.[137] In previous papers Scott suggested that an infection of the sacro-iliac joint was the chief focus, eradication of which by excision or roentgen therapy might stop the spread of the disease. In his current paper he seems to have altered his position somewhat for he stated, "The only explanation of the results [of roentgen therapy] is that these small doses,

given as ' x-ray baths,' stimulate the ductless gland system." In Van Dam's opinion " it is unnecessary to postulate any focus in these joints. The clinical evidence also gives little support."

Treatment. The usual measures were again advocated: removal of infected foci, rest for body and especially for the spine, rest in plaster shells several hours daily, spinal brace, breathing exercises 10 minutes daily to maintain mobility of the costovertebral joints, exercises for hips and shoulders, various forms of physical therapy, and general measures such as cod liver oil.[137, 377] The use of stock polyvalent streptococcal vaccine seemed " justifiable "[137] but its results were unimpressive. Results of treatment with gold salts also were " disappointing " but " more promising than vaccine " according to Buckley who also prescribed calcium gluconate " to make good the calcium wastage." [We strongly doubt the efficacy of such a remedy. —Ed.] The use of forcible manipulation was condemned.[137, 377] Unilateral lumbar sympathectomy was done in one of Buckley's cases of ankylosing spondylitis with painful spasms of legs. " The results were satisfactory and the patient was able to walk better afterwards as well as being relieved of the pain and spasm. The operation will be repeated on the other side, if the improvement is maintained."

[We do not see how lumbar sympathectomy could in any way influence the spinal pathology of this disease.—Ed.]

Roentgen therapy was recommended. According to Van Dam three types of roentgen therapy are used: (1) penetrating rays as used by the majority, (2) the softer rays which are absorbed and are not penetrating, these two types being applied to joints, and (3) irradiation of sympathetic ganglia of the neck in addition to irradiation of the lumbar spine. Gordon and Scott considered deep roentgen therapy " absolutely contraindicated." But Scott was again enthusiastic about his results with " wide field " irradiation. " If the dosage is correct, interesting results are noticed; the patients put on weight, do better work, do not get tired, become symptom-free, etc." He mentioned " striking " results, among them the return of painless " unrestricted movements " four months after treatment in a " hopeless " case of " complete poker back."

[It is difficult for us to share Scott's enthusiasm for such treatment. Although he has written of it for three or four years, he still has published no statistical or clinical details of his results.—Ed.]

Hypertrophic Spondylitis (Spondylitis Osteo-Arthritica)

Clinical Data. This disease was commonly accepted as the spinal equivalent of hypertrophic (osteo-) arthritis in peripheral joints.[137, 982] The well-known clinical symptoms were reviewed.[377, 848] According to Gordon the chief cause of pain and stiffness in these cases is not the osteo-arthritis but its associated fibrositis. Compression of nerve roots results occasionally from osteophytic lipping (which is generally on the anterior surface of the

vertebral bodies well away from the foramina) but more often from dense fibrous cartilage which often spreads extensively round the osteophytes.

[According to Oppenheimer's concept compression of nerve roots is more closely related to the amount of hypertrophic spondylarthritis present than to the amount of hypertrophic spondylitis present.—Ed.]

Cavenagh reported the unusual case of a man, aged 56 years, who had marked hypertrophic arthritis of several cervical vertebrae and extensive bilateral ossification of stylohyoid ligaments.

Treatment. Heat and massage were, of course, generally recommended. Relief of pain following fever therapy was noted by three patients of Bennett and Cash. Terhune approved Hanflig's (1936) method [4] of repeated stretching of the neck in cases of cervical arthritis. "Some measure of relief" was noted by all of 10 patients so treated. Roentgen therapy was approved by Van Dam, but considered by Scott "uncertain in its results." Roentgen-rays of medium wave length were used in early cases with "good results" (Scott). Buckley noted some relief of muscle spasm with deep roentgen therapy.

Gout and Gouty Arthritis

Interest in gout has sharply increased; a few years ago only three to six papers on it appeared annually in English and American literature; about 30 papers were available for this review.

Incidence. From current literature gout seems to be leaving its old homestead in England, and has at last caught up with the children of the Pilgrims in America. English investigators wrote: "Acute classical gout is steadily diminishing" [955]; "tophaceous gout is almost a condition of the past." [18, 19] But in the United States the relative ease with which Cohen, and Vorhaus and Kramer respectively collected 41 and 25 cases of classical gout within a short time convinced them that the disease is common in this country. "The apparent rarity of gout is in reality due to a diagnostic unawareness of it." [992] Van Breemen considered it rare in Holland; there were only seven cases of "old-fashioned gout" among the 20,000 to 25,000 rheumatic cases encountered by him in five years. It is common in Sweden: gout was present in about 10 per cent of the cases of acute polyarthritis and 4.5 per cent of cases of chronic arthritis seen by Kahlmeter in four large general hospitals in Stockholm. The incidence of gout among rheumatic patients at Aix-les-Bains has not changed in the past 60 years; it is still about 1 per cent (seven patients with gout among 800 rheumatic patients). Its incidence in Paris among privately treated rheumatic patients was about 2 per cent, among rheumatic patients treated in hospital 1.2 per cent (Coste, Forestier and Certonciny). Moreno considered gout rare in the Argentine even though the natives are heavy meat eaters. But its incidence among his rheumatic patients was also about 2 per cent. Hill warned that statistics on incidence are difficult to evaluate and dangerous to accept; in the Devonshire Royal Hospital (Buxton) the incidence during 50 years varied notably from

time to time depending on the personal reactions of the changing staff to a diagnosis of gout.

Factors Governing Incidence. Chief factors governing incidence of gout are heredity, sex, age, occupation, personal habits, geography, race, and climate.

1. Heredity. The factor of heredity continues to be most "obvious" among English cases (in 45 per cent of Hill's 93 cases, in 22 per cent of the 54 cases of Gibson and Kersley), much less obvious elsewhere (rare in Sweden [511] and in the Argentine [679]; present in only seven of 120 cases in Vienna [334]; in only four of 41 cases in Philadelphia).[195]

2. Sex. This is again a dominant factor in all series. Gout is rare among females; about 90 per cent or more of the patients are males. In the new series females were affected in the following percentages, 5,[489] 8,[938] 9.8,[195] 10,[334] 11,[359] 20,[861] 22.5,[449] 36.[992] [The statistics in the last three series are distinctly out of line with the common experience and make one suspect the validity of the diagnostic criteria. Among Hill's 93 patients, 21 of whom were females, were 15 with abarticular gout (mostly fibrositis). The clinical description of Vorhaus and Kramer was orthodox enough but no details concerning their nine female patients (out of 25 patients) were given whereby the reader could evaluate the diagnosis. Vorhaus and Kramer gave an exhibit, presumably based on these same cases, at the meeting of the American Medical Association in 1937; at that time some of us could not accept the diagnosis of gout in a few of his cases among women. The condition seemed to be hypertrophic arthritis with Heberden's nodes. Whether these cases were excluded later from his report or whether their inclusion explains the high incidence of females among his patients cannot be stated by us. However, one of the women seen by them had her first attack at the age of 12 years and had many tophi by the age of 27 years.—Ed.] Thomson presented a view commonly held in England, but not in the United States, that gout affects women more often in a nontophaceous, atypical, rather chronic form resembling atrophic arthritis, than in the classical form. In all of Freund's cases of gout among women classical gout with hyperuricemia, recurrent acute attacks of arthritis and complete remission was present. Five women with tophaceous gout were seen,[334, 449, 938, 992] and also a woman with pretophaceous gout whose first attack was at the age of 64 years and whose father had gout (Halsted).

3. Age. Articular symptoms first appeared in most cases between the ages of 35 and 45 years, occasionally in the early twenties.[359, 449, 489, 603] The first attack affected six patients in their teens,[938, 992] one patient at 64 [408] and one at 72 years of age.[359]

4. Occupation. Those frequently affected were "publicans" with opportunities for alcoholic imbibition,[449] and coachmen in England,[980] commercial travelers and railway workers in France.[220] Gout was rare among miners and other workers in heavy manual occupations who are subject to profuse sweating.[449]

5. Personal habits. Those addicted to excesses in food and drink were said to be affected by more numerous and severe attacks, but the disease often affected temperate persons.[408]

6. Geography and race. This factor has been mentioned previously. Gout is rare in colored people. Two American negroes were affected.[142, 195]

7. Weather and climate. According to Coste and Forestier intense cold is bad for gouty patients; it may precipitate acute attacks. In general gouty patients can rarely forecast storms from articular symptoms [938] and no real meteorologic influences were noted in 100 cases of severe gout.[219] However, other studies by Talbott and Coombs suggested that barometric changes affect significantly the metabolism of gouty patients.

Clinical Data. 1. Prodromes. Many patients (50 per cent according to Moreno) experience no prodromal symptoms before an acute attack; some

have dyspepsia and mental depression [956]; others note euphoria [359] or a ravenous appetite as a symptom of the disease.[195]

2. Provocatives. The provocative effects of season, diet, operations, infections, certain chemicals or medicines, and emotional upsets were discussed. Acute attacks occurred most often in spring, much less often in autumn or at other times.[449] In some cases attacks were precipitated by a particular drink or a food not necessarily rich in purine.[359] The female patient of Halsted ate sparingly of meat and rarely took alcohol. Attacks were precipitated by appendectomy in one case, by iridectomy in another.[195] Postoperative attacks were blamed on enforced rest by Van Breemen, on decay of cells incident to operation by Freund. Operations will not always provoke an acute attack, but only in certain cases and at certain times. Thus the patient of Ludwig, Bennett, and Bauer escaped an attack after tonsillectomy within one month of an attack. [Many attacks appear without discoverable provocation. In the experience of one of us, P. S. H., some patients seem to be temporarily more resistant to an attack during the first few weeks after an attack; during this time they are more likely to endure an operation without postoperative flare-up of their gout.—Ed.] Patients with quiescent rheumatic fever may experience a flare-up after any surgical operation but the postoperative exacerbations of rheumatic fever generally occur seven to 14 days after operation [603]; those of gout, usually within five days after operation (Hench, 1935). Acute or subacute coincident infections may provoke acute gout: in one case acute gouty arthritis always developed after an acute "nasal and bronchial catarrh." [359] Shock at the death of a relative, or financial losses suffered by bankers and speculators were cited as precipitants of an attack.[359, 408, 980]

3. Chemical and medicinal provocatives. "Lead gout" (classical acute gouty arthritis precipitated by lead poisoning from drinking water) is still seen in Holland.[980] Injections of gold are said to precipitate attacks in some cases but not in others.[679] The provocative effect of salyrgan was noted previously.[4] Price noted five patients with congestive heart failure, each of whom received on alternate days 1 c.c. of salyrgan intramuscularly and 60 grains of ammonium chloride orally. Within seven to nine days after the first dose copious diuresis of urates and sodium chloride occurred, which was followed at once by acute gouty arthritis. Apparently the salyrgan reproduced disturbances of electrolyte balance similar to those seen in spontaneous attacks by Talbott, Jacobson and Oberg.[3] Three patients given salyrgan by Jacobson had markedly increased quantities of uric acid in urine and decreased quantities in blood, but no attacks were precipitated. To the list of medicinal provocatives previously reported two new ones can be added, decholin (synthetic bile acid, dehydrocholic acid) and thiamin chloride (vitamin B_1). To an elderly gouty patient three weeks after an acute attack Bowers gave decholin (3¾ grains t.i.d) as a choleretic. Within 36 hours after the first dose the joints of both great toes were acutely af-

fected; the drug was stopped and within 48 hours the acute gout disappeared completely.

[This case suggests that decholin may be a provocative, but more information is necessary.—Ed.]

Of special interest are the studies of Vorhaus and Kramer on the effect of vitamin B_1 (thiamin chloride) on gout. The daily oral and parenteral administration of from 1 to 10 mg. (330 to 3,300 international units) promptly provoked acute gouty arthritis in 92 per cent (23) of 25 patients so treated. Attacks usually appeared within two to four, occasionally 10 to 14, days after beginning such therapy and lasted 5 to 10, occasionally 14 days. Reactions were mild in 12, moderate in 8, severe, with fever and disability, in three cases. Despite initial reaction, medication was continued, was thereafter borne well, and seemed of therapeutic value.

[One of us, W. B., has been unable to corroborate these findings.—Ed.]

Acute attacks appeared at night in 84 per cent of Hill's cases. He could not prove the idea that nocturnal attacks occur because a slowed nocturnal circulation presumably favors the precipitation of urates or because at night an increased vagotonia and slight alkalosis supposedly occur. Some physicians are not aware that attacks may or may not be febrile; in current cases temperatures of 102°,[408] 104° or even 105° F. were noted.[859]

Some physicians hesitate to diagnose gout unless a large toe is affected. Podagra (involvement of a large toe) may or may not occur in initial or subsequent attacks. It occurred in the first attack in 15 of Sherwood's 20 cases, in only seven of the 28 cases of Vorhaus and Kramer. A foot was affected in the first attack in 18 of the 24 cases of Talbott and Coombs. Shoulders and hip joints are rarely affected even in late attacks. Shoulders were affected with other joints in one case,[408] hips in three cases,[992] ankles, knees and hips in one case.[603] In Cohen's cases initial attacks were monarticular in 14, polyarticular in 27. In the opinion of the majority, chronic gouty arthritis invariably is preceded by repeated acute attacks with complete remissions.[408, 603, 679, 861] Others [195, 359, 955] stated that gouty arthritis may at times appear insidiously and progress chronically without complete remissions, especially among women.[449] Gibson and Kersley, and Thomson concluded that in some cases classical gout appears at first but develops into a clinical condition indistinguishable from rheumatoid or villous arthritis; hence they suggested the existence of the hybrid, "rheumatic gout," or the coexistence of both gout and rheumatoid arthritis in the same case.

[Such terminology seems to us to increase the existing confusion.—Ed.]

[If such a coexistence occurs, it is extremely rare in our experience.[2] Freund saw one such case. The supposed association of gouty arthritis and nongouty atrophic arthritis in a given case cannot be proved without adequate pathologic studies. In the case of Ludwig, Bennett and Bauer such a combination might have been supposed to exist because spindle shaped joints, ankylosis of several joints and positive streptococcal agglutination tests were present in addition to tophi, but pathologic studies revealed only chronic gouty arthritis in various stages, producing in some joints the general appearance of atrophic arthritis. We agree with Moreno that, because of forgetfulness of minor attacks not considered gouty, some patients erroneously intimate that their gouty arthritis began in chronic fashion.—Ed.]

4. Tophi. Woolner's marks, sebaceous cysts and Heberden's nodes are too often called "tophi." No nodule should be considered a tophus until urate crystals have been discovered therein.[129] Subcutaneous tophi were found in 24,[859] 32,[992] 43,[449, 489] and in 58 per cent [938] of current cases. They are supposedly rare in Sweden.[511] Christopher and Monroe noted a patient

who had had many acute attacks and presented large ulcerating tophi at the heels which five times had been considered to be due to pyogenic ulcers.

Unusual Clinical Features. A patient of Ludwig, Bennett and Bauer had severe tophaceous gout with flexion deformities of knees and fingers, and ankylosis of multiple joints. The condition superficially resembled chronic atrophic arthritis. The patient already had chronic gouty arthritis, having had seven or more acute attacks within five years. Markel reported a case of gout with erythromelalgia; the latter, unrelieved by a regimen for gout, was relieved by injections of typhoid vaccine. Burman performed arthroscopy on the knee of a gouty negro and noted a peculiar fluorescence of the synovial fluid and membrane caused by the presence of bile pigments from mild unsuspected jaundice. Diabetes affected four of Freund's 120 patients.

Irregular Gout. Certain writers accepted the following cases as manifestations of gout: some cases of chronic arthritis without tophi but with transient hyperuricemia,[359] erythema and palmar or plantar hyperkeratosis,[50, 449] certain cases of eczema and urticaria,[50] "gouty" neuralgia, myalgia and sciatica,[1013] trigeminal neuralgia (two cases of the last with hyperuricemia, relieved by colchicine and atophan "when all else had failed"),[449] other conditions supposedly caused by "gouty diathesis" and ranging from so-called rheumatism to eczema.[19] Others noted "indigestion," eczema and pruritus in few or none of their cases of gout.[449, 992] According to Buckley [136] and Thomson, gouty patients suffer so often from fibrositis that the latter may be considered a true symptom of gout. Hill noted 14 cases of "gouty fibrositis" and 21 cases of "gouty arthritis and fibrositis" in which the same biochemical findings and responses to "specific" remedies occurred as in cases of gouty arthritis. A rapid effect from colchicine was noted by seven of eight patients to whom it was given. Gout, however, is rarely the cause of fibrositis: there were only 15 cases of gouty fibrositis "among 8000 to 12,000 cases of fibrositis" seen by Hill. Accepted as gout by Gilbert and Kersley was a case of recurrent lumbago in which the value for blood uric acid was 4.7 to 5.6 mg. per cent. "Neuromuscular tenderness" affected 18 of Vorhaus and Kramer's 25 patients with gout. Many instances of irregular gout ("gouty iritis, gouty phlebitis") have been proved to be due, not to gout, but to septic foci, according to Brown [129] who was "skeptical as to suppressed, and agnostic as to irregular gout."

[We share Brown's skepticism. The data currently presented in favor of the existence of irregular gout continue to be unconvincing. No pathologic studies on tissues related to the symptoms in cases of irregular gout were reported, and only occasionally was precise information given on the effect of colchicine or other remedies for gout.—Ed.]

Complications. Renal insufficiency, generally mild, affected seven of Jacobson's 21 patients. The patient of Ludwig, Bennett and Bauer passed urinary gravel composed of urates in the fifth year of his gouty arthritis. In 25 per cent of Freund's cases kidney stones (generally urate, sometimes oxalate or phosphate) developed; urate stones developed in four of the 24 cases of Talbott and Coombs; renal colic from urate stones occasionally *preceded* the first attack of gouty arthritis.[334, 938] Of itself the passage of urate gravel or stones does not justify a presumptive diagnosis of gout. [But it should certainly initiate a thorough examination of the patient for gout.—Ed.]

Talbott and Coombs found no clinical or laboratory signs of gout in several such cases, and Mann described the symptoms and clinical findings in a number of nongouty patients affected by uric acid showers and renal stones. Of 136 renal stones analyzed by Mann 10 per cent were uratic. Among 50 cases of renal colic Sherwood found five of gout. The pathologic effect of nongouty urate deposits in kidneys was described.[481]

Vascular degeneration is another accepted complication of gout. Marked arteriosclerosis with marked, vascular calcification, visible in roentgenograms, affected the 28 year old patient of Ludwig, Bennett and Bauer.

Laboratory Data. Anemia is usually absent.[861] Gibson and Kersley found slightly reduced volume of erythrocytes, an increased percentage of neutrophiles in differential blood counts, and in Arneth counts a shift to the left even greater in gout than in atrophic arthritis. According to Sherwood " the very nature of gout is incompatible with an alkaline urine. . . . Hence an alkaline urine renders a diagnosis of gout improbable." [We cannot agree with this statement. Alkaline urine is often found in cases of gout. But it might be correct to say that the formation of urate gravel and stones in the renal pelvis and calices (but not in renal parenchyma) is incompatible with alkaline urine.—Ed.] The pH of blood was normal in 125 cases, slightly low in four, increased in only one of Hill's cases. This refutes the theory that in gout the pH of the blood is abnormal. Blood calcium was generally normal.[449]

In many cases the sedimentation rates are markedly elevated (sometimes nearly as much as in rheumatic fever) [511] during acute attacks and rapidly return to normal as attacks subside.[408, 449, 511, 603, 679, 861] Gibson and Kersley found no clinical or statistical relationship between sedimentation rate and level of blood uric acid. In some cases of gout formol-gel reactions were weaker than the sedimentation rates warranted.[359]

Relation of Blood Uric Acid to Gout. Sooner or later practically all gouty patients have hyperuricemia. The concentration of uric acid in whole blood was 4 mg. or more per 100 c.c. (Folin method, 1924) in 59 per cent of the cases of Gibson and Kersley, 4.5 mg. or more (Folin direct method) in about 90 per cent of Hill's cases, and more than 6 mg. (method unstated) in 72 per cent of the cases of Vorhaus and Kramer. Hyperuricemia, however, does not develop in any constant pattern and there is no constant relationship between the duration of gout and the amount of hyperuricemia.[136, 679]

Many patients exhibit hyperuricemia early in the disease,[489, 603, 938] but others may experience several attacks of gouty arthritis, yet exhibit no hyperuricemia.[334, 679, 861] The concentration of uric acid in blood was less than 4.5 mg. in 13 of Sherwood's 20 cases, and " in over 40 per cent of cases of clinically typical gout a high reading [4 mg. per cent or more] was never obtained " by Gibson and Kersley. Patients may even present tophi without hyperuricemia (as in case 3 of Gibson and Kersley). [Such cases are rare.—Ed.] Therefore one must not insist on the presence of hyperuricemia before entertaining a diagnosis of gout.[136, 195, 334, 359, 679, 861]

[Likewise the presence of hyperuricemia is not sufficient for a diagnosis of gout: Gibson and Kersley noted hyperuricemia in 2 per cent of 251 cases of undoubted atrophic arthritis, in 5.4 per cent of 184 miscellaneous nongouty rheumatic cases. The serum uric acid in 3 per cent of Jacobson's 100 nongouty patients was 6 mg. per cent or more.—Ed.]

There is also no constant relationship between the level of blood uric acid and the acute attacks of gouty arthritis.

In some cases the level of blood uric acid apparently increased during acute attacks and decreased thereafter; in others it did not.[136, 195, 449, 1013] Gibson and Kersley noted no constant relationship between sedimentation rates and the level of blood uric acid during acute attacks. Rates were generally increased, but the level of blood uric acid did not rise consistently. Therefore they concluded that if the sedimentation rate indicates the severity of the local tissue reaction, the extent of hyperuricemia must be independent of that process. "The findings appear to indicate that the hyperuricemia is incidental and not an essential part of the disease."

[Nevertheless it is an important feature in the disease.—Ed.]

The concentration of uric acid in serum was compared by Jacobson to that in the whole blood of 21 gouty and 100 nongouty persons. It was concluded that estimations of uric acid in serum (from blood collected and allowed to clot under oil) are more accurate and much less variable than those done on whole blood. Exposure of blood to air appeared to increase the uric acid content not only of whole blood but also of serum. For example the content of uric acid in one sample of whole blood collected in the routine manner and exposed to air was 7.6 mg. per cent; that of a sample of the same person's blood collected at the same time and handled anaerobically was 6.8 mg. per cent. The uric acid in serum of blood clotted in air averaged about 0.5 mg. per cent higher than that in serum of blood clotted under oil. The concentration of serum uric acid (from blood collected under oil) was practically always higher than that of whole blood (collected under oil), but was about equal to that of plasma (handled anaerobically). The new technic was used in determining the levels of *serum* uric acid at different stages of gout in 21 cases during and between attacks. The concentration of uric acid in serum ranged from 5.2 to 14.8 mg. per cent. In about 98 per cent (174) of 177 tests the value exceeded 6 mg. per cent; in 167 tests (about 94 per cent of the total) it exceeded 7 mg. per cent. In four cases the serum uric acid fluctuated markedly both during asymptomatic intervals and during attacks of acute gouty arthritis. Many of the fluctuations were associated with drug (aspirin, colchicine, salyrgan) therapy. In one case, studied intensively for a year, the serum uric acid fell significantly within three days preceding the acute attacks and did *not* rise, but remained unchanged during the attacks. In four cases an apparent direct correlation was found between the highest concentration of serum uric acid and the severity of the disease.

In the cases of Talbott and Coombs the minimal values for *serum* uric acid were 5.7 to 10.4, the maximal values were 6.6 to 14.2 mg. per cent. Gibson and Kersley also compared the uric acid content of plasma and whole blood. In atrophic arthritis values in plasma averaged 0.77 mg. per cent higher, in gout 1.97 mg. per cent higher than those in whole blood.

[When studying these reports on concentrations of uric acid the reader must readjust his ideas on the upper limits of normal: whereas it is 4.5 mg. per cent in whole blood, it is 6 mg. per cent in serum or plasma. In Jacobson's cases of gout the *serum* uric acid was practically always over 6 mg. per cent, but Gibson and Kersley noted values in *plasma* (presumably the equivalent of values in serum) as low as 4.7 mg. per cent. Others of us, M. H. D. and P. S. H., not infrequently have noted values of serum uric acid below 6 mg. in cases of tophaceous, as well as in cases of classical pretophaceous gout. But the method of Jacobson should be called to the attention of laboratory technicians, particularly the colleagues of those concerned with arthritic cases.—Ed.]

The uric acid content of synovial fluid of nongouty controls equalled that of plasma and averaged 1.06 mg. per cent higher (range 0.2 to 2.0 mg. per cent) than that of whole blood (Gibson and Kersley).

In the case of Ludwig, Bennett and Bauer during attacks of gouty arthritis the urinary uric acid increased notably, but there were no consistent changes in the serum uric acid: The mean value for serum uric acid during attacks was 12.4 ± .2 mg. per cent, between attacks 12.1 ± .3.

Roentgenograms. These are of little diagnostic value in early stages of gouty arthritis.[511, 532] They may be " negative," as they were in 50 per cent of Sherwood's cases, or they may show a variety of nonspecific changes as they did in 96 per cent of the cases of Vorhaus and Kramer. In the latter the average duration of the gout was seven years among patients with slight roentgenographic changes, nine years among those with moderate changes, and 11.6 years among those with marked changes. Weissenbach and Françon gave the name " thorn foot " to the [nonspecific hypertrophic] exostotic reactions in articular bone at the upper surface of the tarsus in seven cases. When roentgenograms become really helpful the diagnosis is generally obvious on other grounds.[511] In the severe case of Ludwig, Bennett and Bauer a variety of " specific " and nonspecific hypertrophic and destructive changes appeared, and three unusual features: ankylosis of several joints, involvement of a sacro-iliac joint and small areas of erosion at the articular surfaces of femur and tibia at a knee joint. Areas of erosion at large joints are " extremely rare "; for diagnosis one should obtain roentgenograms of hands and feet and not rely on those of large joints. Even so areas of erosion are not necessarily gouty, but may occur in cases of atrophic and hypertrophic arthritis, lupus pernio and cystic diseases of bone (Golding). Hence roentgenographic changes, although helpful, should never be considered final or conclusive evidence for gout.[859, 980]

Pathology. It is not easy to find in American literature descriptions of the pathologic reactions of gout. The articular changes in their case were described in detail by Ludwig, Bennett and Bauer. To preserve the specific gouty (uratic) lesions the tissues must be fixed, not in formalin or the usual formalin-containing fixatives (which rapidly dissolve the urates), but in absolute alcohol and stained with silver nitrate (de Galantha method[3]). Sodium urate crystals may be deposited in cartilage, synovial membrane, perichondrium, subchondral bone, bone marrow, periosteum, fibrous capsules, adjacent ligaments, tendons and bursae, especially the olecranon bursae. Wherever the deposits occur they invoke a foreign-body, giant-cell reaction with proliferation of fibrous tissue and small collections of lymphoid cells. The extent of articular change that occurs depends on the amount of urates deposited, their situation and the resultant reaction to them. These reactions may include regional destruction of cartilage and subchondral bone, overgrowth of cartilage and bone (" hypertrophic arthritis ") at articular margins, synovial fibrosis and formation of pannus which may (rarely) cause ankylosis. The pannus is studded with urate deposits which distinguish such a pannus from that of atrophic arthritis.

Vascular sclerosis may occur in the region of urate deposits and elsewhere. Notable arteriosclerosis was present in the legs of one 28 year old

patient.[603] The finding of such changes supports the aphorism of Huchard that gout is to the arteries what rheumatic fever is to the heart. Hill regarded the various forms of arrhythmias and anginal pain seen in gout the result of myocardial ischemia from coronary sclerosis and not due to specific gouty lesions.

"Gouty teeth," yellow worn-down teeth with exposed dentures, have been considered signs of a gouty constitution. But Gibson and Kersley[531] saw nongouty persons with such teeth, and gouty patients without them; they found no histologic difference between the teeth of gouty and nongouty persons.

Diagnosis of Gout. The fact that in one series of 25 cases an average of 8.8 years elapsed between the first attack of gouty arthritis and the first diagnosis of gout constitutes an indictment of the prevailing attitude toward gout (Vorhaus and Kramer). Physicians currently do not think of gout or will not make the diagnosis unless a big toe is affected or hyperuricemia or even tophi are present. Absence of these features in a given case, however, must not prevent a diagnosis of gout if other significant data are present.[334] The commonest source of error is an incomplete case history.[195] The most important single diagnostic feature is an accurate history describing the characteristic features of the single attack and the continuing pattern of acute attacks with complete remissions.[359, 603, 956] The delayed excretion of uric acid by a patient on a diet rich in purines was considered of no diagnostic value; such delays also occur in cases of atrophic arthritis and are nonspecific (Freund). The provocative tests used by Gibson and Kersley gave inconclusive results. Ketogenic diets were given in seven cases of gout (and in three control cases): moderate ketosis resulted but no change in the concentration of urinary uric acid. Among 11 gouty patients given a ketogenic diet the blood uric acid increased moderately but only three had "more discomfort" and only one an acute attack. Thus a ketogenic diet could not be used as a hard and fast provocative test in borderline cases. For periods of a week each, stimulants of the sympathetic nerves (ephedrine and bellafolin, an atropin preparation) and of the vagus (ergotamine tartrate) were given in unstated amounts: of eight patients so treated six noticed no change; only two noted any real change—these were better from the sympathetic, worse from the vagal stimulants. Therapeutic tests, such as relief with cinchophen or with diet, are not sufficiently specific to be of unquestioned diagnostic value. The most convincing and specific test is "the quick answer to colchicum" (Moreno).

Etiology. No new ideas on etiology were reported. Most writers now believe that the hyperuricemia is not the cause of the disease but only a symptom[129, 532, 956, 1013] and that gout is a metabolic disturbance of some sort possibly related to hepatic dysfunction.[135, 954, 980, 1013] The human liver is notably concerned with the formation of uric acid. Hepatic enlargement,[195] epigastric heaviness and oppression possibly caused by hepatic con-

gestion,[449] and abnormal results of levulose tolerance tests of liver function were frequently,[265] but not consistently, noted. Thomson suspected that a hepatic dysfunction might be induced by failure of some activating hormone of external origin. The fact that gout usually attacks men suggests some endocrine factor. But so far no direct evidence thereof has been found.[265]

The presence of an allergic factor was suggested again.[136, 531, 1031] Perhaps acute attacks are due to bacterial or food sensitivity: cited as evidence was the case of a patient whose attacks were provoked by cider but not by alcoholic beverages.[359, 532] Gouty patients, however, do not exhibit the usual types of allergic reactions.[359, 449] Aschoff found no evidence that sensitization of articular or renal tissues exists in gout: "It is impossible to speak of an allergic inflammation in an attack of gout."

The infectious theory received no support: infections merely act as predisposing or provocative factors.[265, 359] The idea that gout results from hyperuricemia caused by some primary renal insufficiency also received no support.[449, 938, 956] Gout often causes, but does not result from, nephritis.

Pathogenesis. Gout must be regarded as a chronic disease; the arthritic attacks are merely its "acute explosions."[408] Hyperuricemia is one of the results, not the cause, of the disease. Is it due to (1) excess formation, (2) deficient excretion, or (3) diminished destruction of urates in the body? Modern writers favor the first idea.[136, 938] Talbott and Coombs found no evidence to support the second or third ideas. Indeed both during and between attacks several gouty patients (unless they had advanced renal damage) excreted more urates than did their nongouty controls. In gout most of the uric acid in human blood or other bodily fluids is either excreted or deposited, according to Talbott and Coombs, who stated that in this disease there is increased formation of uric acid. They continued the work of Talbott, Jacobson and Oberg [8] which indicates that many chemical changes besides those concerned with uric acid occur in gout.

Cyclic variations in urinary volume and content, in the body weight and in insensible loss of perspiration occurred among both gouty and nongouty persons but that of the gouty was of greater magnitude. In the latter, cyclic variations occurred during both the symptom-free periods and the arthritic attacks. Talbott and Coombs noted (as did His, 1899, and Futcher, 1914) that prior to acute attacks a diminished urinary output of uric acid occurred; then about 24 to 72 hours before acute attacks diuresis with an increased concentration and excretion of various urinary constituents, especially sodium and chloride frequently occurred. This diuresis continued during the first few days of the arthritic attack, and was greatest usually just before or on the day of the greatest articular distress, at which time the output of fluid was about twice that prior to the diuresis and was accompanied by an increased excretion of urates. Subsequently as the cycle continued there was a diminished excretion of water, salt and urates. During the diuresis the patients paradoxically gained weight because of a significant reduction in their insensible loss of fluid. Gouty patients do not seem to be affected much by changes in weather and Talbott and Coombs noted no relationship between these clinical and chemical cycles and changes in external temperature and humidity, but they did note that a fall in barometric pressure practically always preceded diuresis by about 12 hours when there were no articular symptoms.

by about 12 to 24 hours when acute attacks occurred. The significance of these observations is not clear.

Treatment of Acute Attacks. The use of a brisk mercurial purge at the onset of the attack and a saline purge on alternate days during the attack was recommended.[136, 956] Compresses should be applied to the affected parts: either hot wet packs,[956] a cataplasm of kaolin, a lotion of soda bicarbonate, opium and belladonna,[136] or saturated solution of magnesium sulfate.[195] The most effective remedy is colchicum, given as the wine (15 to 20 minims every two to three hours) or as colchicine 1/120 or 1/100 grain every one to three hours until articular symptoms subside or gastrointestinal symptoms appear.[106, 136, 603, 956] Bowers gave colchicine 1/100 grain six to eight times daily for two to three days. Talbott and Coombs gave colchicine 1/120 grain every one or two hours for 8 to 16 doses depending on the patient's tolerance and the severity of the attack. The mechanism of the action of colchicine in gout is obscure and is not explained by the recent interesting studies of its cytotoxicologic effect.[559, 582]

Variable diets were used: a "purine-free diet," [956, 980] a "soft diet" [938] or one which avoids foods rich in purine.[603] Cinchophen was not used by some,[603] used with due precaution by others in those cases in which salicylates [359] or colchicine [956] does not give relief, and then only if results of liver function tests are normal.[136, 956] On the days on which cinchophen was given, extra amounts of sugar and water,[359] and sufficient alkali to keep the urine faintly alkaline were prescribed: sodium bicarbonate 30 grains t.i.d.[956] or potassium bicarbonate 30 grains t.i.d.[136] Some approved the use of salicylates or aspirin when cinchophen was contraindicated [136] but others considered salicylates of doubtful value except as an analgesic.[956] The use of salicylates after the method of Jennings [5] failed to control the gout in two cases in which it was controlled later by cinchophen.[359, 582]

Crystalline thiamin chloride (vitamin B_1) was given orally and parenterally (from 1 to 10 mg.; i.e., 330 to 3,300 international units daily) by Vorhaus and Kramer to 25 gouty patients. Despite the initial, acute exacerbations mentioned heretofore, it was given for from 3 to 36 months. Hyperuricemia was *not* controlled thereby; in some cases it increased, but "a definite change in the frequency and intensity of their disease" was noted. Results were marked in 11, moderate in 9, slight in 2, absent in 3 cases. This therapy has since been used by Kuhnau, Schroeder and Wolff (1937).

[One of us, W. B., was unable to corroborate these results.—Ed.]

Spa therapy is contraindicated during acute attacks,[696, 955, 956] but warm soda baths were considered excellent.[980]

Interval Treatment to Prevent Attacks. The occasional use of a mercurial purge and the frequent use of mild saline cathartics were approved.[136] In cases in which more than two attacks occurred yearly, colchicine, 1/120 grain t.i.d., was given for two or three days each week by some,[136, 938] for one

out of every four weeks by others.[195] Jacobson occasionally noted an apparent reduction in values for serum uric acid after use of colchicine, but because of great fluctuations in values for serum uric acid among untreated patients the effect of colchicine on hyperuricemia could not be determined finally. Others [129] accepted the older view that colchicine has no effect on uric acid in blood or urine and is powerless to avert attacks.

The intermittent use of cinchophen after the method of Graham (1927) was approved by Bower, but used by Cohen only for patients who did not tolerate colchicine (which he considered as effective a prophylactic as cinchophen). Cinchophen was considered more dangerous than valuable by others,[603, 938] but despite occasional danger Brown,[129] who was one of the first to describe cinchophen toxicity (1926), concluded that gouty patients should not be deprived of "its undoubted benefits." In lieu of cinchophen others prescribed 60 to 80 grains of aspirin daily for 4 days each week,[603] or neocinchophen 7½ grains t.i.d. for two days a week intermittently.[408] Aspirin seemed to reduce the level of serum uric acid occasionally.[489]

Dietary prescriptions varied considerably. Some [489, 603, 938] considered purine-low diets of unproved value and ineffective in controlling hyperuricemia at least when used for three months or less. Others regarded purine-free or purine-low diets effective if used long enough.[135, 195, 221] It was agreed that all alcoholic beverages including beer and in some cases cider also should be avoided.[135, 136, 956]

Many gouty patients are convinced that an annual or semi-annual visit to a favorite spa constitutes an effective prophylaxis against acute attacks.[18, 19, 136] Spa therapy was considered strictly contraindicated in acute attacks, but of value to gouty patients with little or no articular symptoms. The mild forms of hydrotherapy (vapor baths, brine baths) were considered safe but other forms must be avoided or used with caution lest they provoke acute attacks, "bath reactions" or "cure-crises." [43, 696, 955, 956]

Additional Treatment. Infected foci should be removed (for other than local reasons) in cases in which acute infections therein appear to provoke attacks of gout.[334] Occasionally it is easier to control a case of gout when some infected focus is removed.[136] For chronic gouty arthritis roentgen therapy or [511, 1016] ionization with lithium iodide [44] was recommended. [No results given.—Ed.] Excellent healing almost always results when ulcerating tophaceous deposits are adequately curetted.[859]

Prognosis. Gout was called a wretched, but tiny error of metabolism, not fatal to life (Van Breemen). Once the disease is present, it persists throughout life. There is no cure for it (Buckley; Talbott and Coombs). Some [603] are doubtful if any regimen materially affects the course of the disease, alters its relentless progress, or prevents acute attacks. An annual exacerbation of gout is to be expected, according to O'Reilly.[728] But most physicians have concluded that constant treatment accomplishes much in providing symptomatic relief and modifying the number and severity of

attacks.[136, 938] Some of Cohen's patients who had had frequent, repeated attacks for years, remained free of attacks for as long as seven years when they kept on their regimen.

Cinchophen Toxicity

Between 1913 and 1935, 190 cases (107 nonfatal, 83 fatal) of toxemia from cinchophen or its derivatives were reported throughout the world. A survey of these cases by Bryce [133] indicated that persons over 40 years of age are more susceptible to toxic reactions than those younger, and that females are affected more frequently and have a smaller chance of recovery than males. In view of the quantities of phenylcinchoninates consumed throughout the world Bryce [134] considered cinchophen intoxication comparatively rare, and the frequency of fatal acute hepatitis from these drugs "extremely low." [132] According to his estimate the *minimal* empiric chance of *any toxic reaction* from a single dose of cinchophen or neocinchophen is about 1 in 7,500,000; and that of *fatal intoxication* from a single dose is about 1 in 15,000,000. Similarly he estimated that the *maximal* empiric chance of *fatal intoxication* is about 1 in 60,000; that of *any* intoxication is about 1 in 30,000. Bryce concluded that somewhere between these extremes lies the "true" figure representing the empiric chance of intoxication.

[Deaths from cinchophen toxicity reported in the literature probably represent only a fraction of the actual number that have occurred. Therefore it is not possible to say how correct Bryce's estimate is.—Ed.]

Sugg also admitted that minor forms of cinchophen toxemia affect only a small percentage, and fatal intoxication affects only a fraction of 1 per cent of those who use it, as far as reported cases are concerned, but he expressed the belief that many cases, even fatal ones, go unreported and the condition goes unrecognized because physicians are still not sufficiently aware of the dangers of cinchophen and related compounds. Especially are they unaware of the fact that delayed or acquired sensitivity can occur; hepatic injury therefrom can first manifest itself many months after use of the drug has been discontinued. From the literature Sugg collected 26 cases, to which he added six, in which no toxic reaction occurred when the drugs were first given, even in large doses for long periods, but in which toxic reactions accompanied or followed later courses of the drugs. Cutaneous reactions affected 12 patients, 2 fatally; hepatic reactions affected 22 patients, 12 fatally.

The mechanism of such toxic reactions in humans is unknown. They may be due to allergy of the liver, or to the superimposition of the choleretic action of cinchophen on present or previous liver damage.[134, 928] The continued administration of cinchophen to dogs produces a chronic gastric ulcer similar in appearance and situation to human gastric ulcers; but no such ulcerous formation occurs in man (Bollman, Stalker and Mann; Simonds).

The Uric Acid Problem

Certain amino acids, pyruvic acid, and glucose increase the excretion of uric acid; fats decrease it. Insulin increases the output of allantoin in dogs; it also increases the concentration of uric acid in blood and urine in Dalmatian hounds, but not their urinary allantoin. This is probably due to the mobilization of adrenalin by insulin: injections of adrenalin increase the uric acid content of blood and urine in Dalmatian hounds (Larson and Chaikoff, 1935). These studies were extended by Miller and Kuyper. The injection of insulin or adrenalin into rabbits increased the excretion of uric acid. Insulin apparently exerted its effect indirectly by lowering the blood sugar and causing mobilization of adrenalin. Adrenalin appeared to affect purine metabolism first, but protein catabolism as a whole may also be stimulated. The administration of 30 to 40 units of insulin to a normal person and to three diabetics produced no significant changes in uric acid content of blood or urine; neither did injections of 0.5 to 1 mg. of adrenalin. But when Rosenberg gave larger doses (65 to 100 units) of insulin to nine men, marked reduction in the level of blood uric acid occurred; the reduction in some cases amounted to 50 per cent or more. For example the level of uric acid of whole blood of one patient, given 100 units, fell from 2 to 1.3, that of plasma from 4 to 2.3 and that of serum from 5.4 to 1 mg. per cent. No urinary studies were reported. The decrease in blood uric acid was independent of the appearance of hypoglycemia: it occurred when hypoglycemia was permitted to develop and also when it was prevented from occurring by the administration of carbohydrate.

[Further work will be necessary to determine whether these studies can be applied to the problem of gout. The effect of insulin on blood uric acid was transient: values returned to normal within about six hours. The doses, given by Rosenberg mainly to schizophrenics, were larger than those generally given to diabetics. But these studies are of interest in connection with the case reported by Rabinowitch (1928) in which acute gout was repeatedly precipitated by injections of insulin, the only case of the kind we know of.—Ed.]

The uric acid content of blood and urine in Bright's disease was studied by Brøchner-Mortensen. The clearance of uric acid was compared to that of urea and creatinine. Despite significant renal insufficiency uric acid clearance was often normal. Usually retention of uric acid occurred only after considerable retention of urea; in severe cases the retention of urea was relatively much greater than that of uric acid.

[This is further evidence against the notion that gout may be a symptom of early nephritis.—Ed.]

To determine the "true uric acid" content of blood Blauch and Koch made determinations on plain serum and on similar serum after incubation with the enzyme uricase (from ox kidney) which specifically destroys uric acid. The difference in the two values was regarded as the "true uric acid." The average value of uric acid in 25 samples of human blood was 3 mg. per

cent before treatment, and 0.8 mg. per cent after treatment with uricase. Hence the true value of uric acid was 2.2 mg. per cent.

The purine metabolism of Dalmatian coach hounds was studied by Young, Conway and Crandall. Variations in the protein, amino acid and purine contents of their diets caused considerable variation in the output of allantoin but little change in that of uric acid. Apparently formation of uric acid in these animals is almost entirely endogenous and independent of the diet. The dietary purine is converted to allantoin and excreted as such. By studying the offspring of Dalmatian hounds ("high uric acid excretors") mated with collies ("low uric acid excretors") Trimble and Keeler noted that "high uric acid excretion" is inherited as an almost completely recessive, nonsex-linked character, dependent for its expression on the presence of a single pair of mendelizing genes. The genes underlying the "high uric acid excretion" and those underlying the production of Dalmatian spotting are resident in independent pairs of chromosomes.

[Such studies could and should be carried out on gouty families, particularly on the offspring of the union of a gouty and a nongouty person. Children and other relatives of patients with gout may demonstrate notable hyperuricemia without (other) symptoms of gout, according to Folin and Denis, 1915, and Jacobson.—Ed.]

Psoriasis and Psoriatic Arthritis

It has been stated, among others by Hunt,[1] that patients with chronic rheumatic diseases frequently exhibit psoriasis. In further studies Hunt noted a family history of various rheumatic manifestations in 70 per cent of 75 cases of psoriasis. According to her the following features characterized the supposed relationship between psoriasis and "rheumatic infections": (1) eruption on the skin following the appearance of rheumatic infection after "a latent period of some weeks," (2) a distinctive eruption, widespread guttate and nummular lesions resembling a secondary syphilid, (3) immunity in later life from the more serious rheumatic complications such as valvulitis. In contrast to Hunt's views Pringle considered the coexistence of psoriasis and rheumatic diseases uncommon. Among 2000 consecutive cases of "rheumatic disease" psoriasis occurred in only 17; of these 17 patients one had "subacute rheumatism," four had fibrositis, six had atrophic arthritis, three had hypertrophic arthritis, and three had "chronic villous arthritis." Among an additional 500 patients with rheumatism only three had psoriasis, making the incidence of psoriasis among 2500 rheumatic cases only 20 (0.8 per cent).

Two different relationships between psoriasis and rheumatism were cited by Barber: that in which the two were concurrently associated, and that in which the two conditions alternated. He stated that he had met several psoriatics who refused treatment for their eruption because its disappearance left them crippled with rheumatism. He regarded psoriasis as common in atrophic arthritis: "Of course psoriasis is so common a disease that its fortuitous occurrence with arthritis and other rheumatic disorders might be expected." But the association is "too frequent to be a coincidence." The special association, "psoriatic arthropathy," was considered by him "a well-

defined syndrome" characterized especially by the peculiar tendency for involvement of terminal phalangeal joints of fingers and toes with psoriasis of adjacent nails [a point of diagnostic importance previously described by one of us, P. S. H.[8]—Ed.] Also, according to Barber, in psoriatic arthritis, the progression of the articular lesions is generally less rapid, less continuous, and less relentless than in nonpsoriatic arthritis, so that despite some years of the former disease articular deformities and crippling may be slight.

There were 26 cases of psoriasis among about 1000 cases of atrophic arthritis (an incidence of 2.6 per cent) but only three cases of psoriasis among more than 1000 cases of hypertrophic arthritis studied by Dawson and Tyson. Hence the association of psoriasis with atrophic arthritis was considered "of real significance." The term, "psoriatic arthritis," has been applied by some workers to the combination of psoriasis with almost any form of rheumatism, and by others to the association of psoriasis with atrophic arthritis. Still others have used the term in a much more restricted and special sense to describe, not psoriasis with atrophic arthritis, but a form with characteristics which set it apart, perhaps, as a specific entity. Of the 26 cases of psoriasis and atrophic-like arthritis seen by Dawson and Tyson 12 were listed as "classical psoriatic arthritis" with features unusual for true atrophic arthritis but supposedly characteristic of psoriatic arthritis (involvement of terminal phalangeal joints in six, psoriatic nails in eight, asymmetrical arthritis—isolated joints being involved apparently at random—a relationship between the onset and activity of the skin and articular lesions which was fairly close in some, less close in others). Eight of the 26 cases were regarded as less typical examples of psoriatic arthritis, in general resembling ordinary atrophic arthritis and exhibiting no involvement of terminal phalangeal joints. The remaining six cases were regarded as cases of typical atrophic arthritis with coincident psoriasis. Because they could draw no sharp line of distinction between the three groups Dawson and Tyson regarded psoriatic arthritis as still an uncertain entity.

Two of Hench's patients with psoriatic arthritis were markedly relieved of their articular symptoms during pregnancy,[431] but pregnancy was listed by Ingram as one of the precipitating factors of acute psoriasis.

[These various reports reveal the confusion that exists about this supposed entity, and some of them increase rather than lessen the confusion. The question as to whether psoriasis is frequently associated with a variety of rheumatic diseases must be kept distinct from that as to whether a special form of arthritis with psoriasis exists which is distinctive enough to be called "psoriatic arthritis" rather than "atrophic arthritis with psoriasis." In neither of her papers (1933, 1938) did Hunt describe anything resembling the symptom-complex to which some restrict the term "psoriatic arthritis." Much more work must be done before the clinical boundaries of "psoriatic arthritis" can be drawn (if ever) with final accuracy. Meanwhile, three of us accept the entity, the others do not.—Ed.]

Because terminal phalangeal joints are frequently affected in association with psoriasis of adjacent nails physicians should distinguish psoriasis of nails from other ungual lesions. Ingram considered it impossible for one to diagnose psoriasis of the nails without the presence of psoriasis elsewhere. But Crawford and White con-

sidered the psoriatic nail lesions distinctive enough for recognition. Of Crawford's 231 cases of psoriasis 50 per cent presented psoriasis of nails. Fingernails were affected almost twice as often as toenails. The latter were never affected without lesions of fingernails. The principal changes in nails seen, in order of frequency, were pitting, changes in the color of the nail plate (present in about 66 per cent of 1277 affected nails), thickening of the nail plate, longitudinal ridging and erosion. The histologic picture was analogous to that of epidermal psoriasis. According to White psoriasis can occur in the nails alone, and the order of appearance of the nail changes in his cases was: (1) detachment of the nail, (2) partial parenchymatous alterations likely to end in partial destruction of the nail, (3) color changes, (4) shortening of the nail, (5) nail puncta. "The existence of these psoriatic erosions proves incontestably that psoriasis is a disease of internal origin and that the causal agent begins to multiply at the nail matrix, led there when the psoriasis passes into the erythrodermic phase and attacks the fingers. . . . Transverse lines appear and these usually indicate the initial onset of generalized psoriasis."

[No mention of articular lesions in joints adjacent to affected nails was made by Ingram, Crawford, or White.—Ed.]

Etiology. Theories on the etiology of psoriasis were discussed. According to Ingram there is no evidence that psoriasis is an infection, and very little to support the recent German view that it is due to a disturbance of fat metabolism. Reiss concluded that there was a decreased excretion of vitamin C in psoriasis from the disturbed cellular metabolism of the epidermis.

Treatment. No comments on the treatment of psoriatic arthritis were given, but control of psoriasis of skin and nails has been considered of first importance. The relative value of various remedies was discussed: for nails roentgen therapy and doses of arsenic (internally) alone or in combination[1028]; for the skin tar baths and artificial sunlight or cignolin inunction, protein shock, occasionally chrysotherapy.[483] Despite the vitamin C deficiency noted by Reiss the administration of vitamin C (redoxon) caused improvement in only two of his 13 cases of psoriasis (joints not mentioned). Injections of thorium X given "with great prudence," were considered useful (Weil and Bach). Following the work of others[4, 5] Brunsting used massive doses (average 300,000 units) of vitamin D (ertron), daily for 1.5 to 7 months. Two of 19 patients so treated had associated arthritis [but it was not materially benefited.—Ed.]. The psoriasis cleared entirely in three, was markedly improved in seven cases, was not significantly benefited in the rest. In three cases nausea and headache occurred; in none was there marked hypercalcemia. The results were "encouraging" but less striking than those reported by Cedar and Zon[5] who used crystalline vitamin D. Perhaps some forms are more potent than others.

Hemophilia and Hemophilic Arthritis

No articles on hemophilic arthritis appeared.

Further studies on the use of extracts from fresh normal serum and from placenta, both of which contain coagulation-promoting substances related to protein, were reported by Bendien and Van Creveld, and by Pohle and Taylor. Three patients

with hemophilia were treated by venesection with results "surprising" to Lawson and Graybeal who felt that possibly the hemorrhagic crises were an effort of nature for relief. For seven years, in one case, about 500 c.c. of blood were removed every 6 or 8 weeks or whenever fullness in the head or pains in joints appeared.

Allergic Arthritis

In the usual vague way "allergy" was blamed for chronic polyarthritis. According to Keating "there are allergic joints, as there are allergic chests, intestinal tracts and other mucous membranes. Many patients have acute arthritic symptoms only following the ingestion of certain foods. . . . Arthritis frequently has a primary metabolic or endocrine basis upon which may be superimposed allergic manifestations to certain bacterial toxins or foods." The features of this so-called allergic type of arthritis were presumed to be the following: the joint symptoms are mildly progressive in type but occasionally become very acute. The spine as well as some of the larger joints is affected. Exacerbations are of short duration and are accompanied by mild gastrointestinal symptoms. Hydrops is not uncommon. Roentgenograms in early cases do not reveal any abnormality but later frequently reveal "changes suggestive of a mixed atrophic and hypertrophic type." [It would be difficult to identify "allergic arthritis" from this description. No clinical or pathologic proof of such an entity was given.—Ed.] Already mentioned was the report of Pottenger who stated that patients with atrophic and hypertrophic arthritis possess a hereditary tendency to allergy, exhibit food sensitivity in 90 per cent of cases, and "almost universally" manifest specific sensitization in various tissues. "The type of reaction in the joint suggests an allergic reaction."

In determining whether a disease belongs in the allergic group Gutmann applied these criteria: (1) determination of the suspected allergen by the skin test or the Prausnitz-Kuestner test (passive transfer of sensitivity), (2) disappearance of the symptoms when the allergen is removed, (3) reappearance of symptoms following re-exposure to the allergen. Omitting the so-called infectious-allergic conditions (rheumatic fever, arthritis with tuberculosis and other infectious diseases), Gutmann recognized the following "allergic arthropathies": (1) genuine allergic arthritis, (2) joint swellings in serum disease, (3) "hydrops articulorum intermittens, angioneurotic edema fugax of Quincke," (4) "periarthritis, tendovaginitis," (5) purpura, (6) "gout, arthritis urica, psoriasis," (7) "rheumatism." He considered true allergic arthritis a "relatively rare" disease and cited two cases.

In case 1 a patient who had previously had "gall-bladder inflammation" (severe pain, vomiting, no fever or abnormality visible in roentgenograms) had repeated episodes of urticaria which disappeared when wheat flour and fish were avoided. Later after eating toast (wheat flour) and a salad containing fish she had pain in the region of the gall-bladder, itching of the entire body "without urticaria" and excruciating pain with swelling of a knee joint, but no fever. The red, swollen, painful knee required splinting. "It could be demonstrated that the eating of fish was the cause of the gall-bladder and knee joint symptoms, and that following the ingestion of wheat

flour urticaria occurred." [But the writer just said that itching occurred without urticaria.—Ed.] "However, while the urticaria and the gall-bladder symptoms quickly receded, the inflammatory condition of the knee joint continued for several weeks before it finally disappeared. The most striking proof of the allergic nature of the arthritis was the effect of eating fish."

In case 2 the patient had frequent short attacks of pain in the back, torticollis and lumbago. Later "spondylitis deformans" and intolerance to certain foods, nausea after eating boiled eggs, and diarrhea after drinking milk developed. "Allergy tests" revealed hypersensitivity to milk but not to butter, eggs or tobacco. Pains "definitely decreased" when milk, tobacco and eggs were avoided, later were intensified when milk and tobacco were allowed. "Milk and tobacco were again withdrawn and the pains decreased. As a result the spine became more mobile. Definite and continued improvement was evident after about one year."

Gutmann also cited two cases reported by Adelsberger and Munter (reference not given) caused by eggs and meat, and the case of Lewin and Taub [4] caused by English walnuts.

Examples of the other types of so-called allergic arthropathies were also given.

[We are not opposed to the idea that certain probably rare forms of acute recurrent or chronic arthritis may represent allergic reactions to certain foods, but most of the case reports of allergic arthritis leave much to be desired. Important details are often omitted, particularly precise details about the condition of joints when the offending foods are given or withdrawn. So often the evidence is unconvincing that the articular lesions subsided with significant rapidity and completeness when the offending antigen was avoided, and the clinical distinction between "allergic arthritis" and the ordinary forms is generally vague. Photographs and roentgenograms of the joints should be published; needed most of all are studies on the pathology of the condition.—Ed.]

"Metabolic Arthritis"

This term was not used in the literature under review.

Endocrine Arthritis

Menopausal Rheumatism, Arthralgia and Arthritis. Of 1000 women suffering from various menopausal symptoms 24 per cent complained of rheumatic pains ("arthritis and fibrositis").[222a] Long debated has been the question as to whether the menopause merely acts as a predisposing factor to the development, late in life, of any one of several common forms of arthritis, whether it can be the direct cause of such forms as atrophic or hypertrophic arthritis or whether it is responsible for a special type of true menopausal arthritis different clinically and pathologically from all others. For years "villous arthritis" has been offered as the true menopausal or climacteric arthritis. But since there has been no agreement as to the clinical or pathologic picture of menopausal arthritis and no experimental or clinical proof that any glandular dysfunction alone can cause arthritis, American physicians have in general refused to accept any form of menopausal rheumatism. According to present concepts the characteristics of the menopause are sup-

posedly (1) cessation of estrin secretion, (2) then overactivity of the anterior pituitary gland resulting in a flooding of the body by excess prolan, (3) coincident overactivity of the thyroid gland and adrenal medulla. In some women the normal endocrine balance is upset less violently by the menopause and a new balance is established more readily than in others. It has been suggested that sometimes the menopause is characterized by pituitary failure, not pituitary stimulation (Hall) and by a deficiency, not an overactivity, of thyroid (Stone). Thus there may be more than one type of menopause, and if so there may be more than one type of menopausal rheumatism.

[The differences in menopausal biochemistry are probably more quantitative than qualitative.—Ed.]

Those who accept the idea that the menopause is related to one or more joint disturbances have conceived of the following possibilities. By acting as a predisposing factor the menopause may be the *indirect* cause of any one of several common forms of rheumatism including atrophic or hypertrophic arthritis and fibrositis, or the menopause may be the *direct* cause of a variety of forms of menopausal rheumatism such as the following: (1) polyarticular hypertrophic arthritis ("menopausal hypertrophic arthritis") presumably due to the thyroid deficiency of the menopause, (2) polyarticular atrophic arthritis ("menopausal atrophic arthritis"), (3) polyarthralgia ("menopausal arthralgia"; stiff, sore joints with or without mild subcutaneous edema, but not a true arthritis) presumably due to a deficiency, not of thyroid, but of ovarian secretion, (4) menopausal fibrositis (stiff, sore muscles; tender subcutaneous fibrofatty nodules), (5) "villous arthritis," a special form of arthritis with distinctive pathologic reactions confined almost exclusively to knees.

1. "Menopausal arthralgia." The characteristics of this condition as seen by Hall in 53 cases included: freedom from joint symptoms until after artificial menopause; then the appearance of joint pain, stiffness and tenderness with no true articular swelling but with slight subcutaneous edema, full motion and no deformity; generally normal sedimentation rates; occasionally low metabolic rates; *aggravation* of menopausal symptoms by thyroid therapy; relief of menopausal symptoms and joint pains with adequate doses of estrogenic substance; return of joint pains when estrogenic substance was discontinued or substituted by a placebo. The articular symptoms were worse after rest and sleeping, better after moderate, but worse after excessive, physical activity. Thus some might call the condition periarticular fibrositis. Coincident hypertrophic arthritis affected one-third of Hall's patients. No pathologic studies were made but the disturbance was believed to be, not a true arthritis, but one in periarticular tissues. In some cases pain was chronic and mild or moderately intense; in others it was severe and spasmodic, perhaps from vascular spasm.

Treatment. Intramuscular injections of progynon B were given twice weekly; doses varied considerably and failures were usually due to inadequate

dosage; as a rule 10,000 international (2000 rat) units were sufficient if continued at least four to six weeks, but in some cases 50,000 international (10,000 rat) units were required. Single doses were rarely effective; generally no effect was noted until after three to six weeks of treatment. Of the 53 patients so treated 40 were "adequately treated"; of them 80 per cent were materially ("50 to 100 per cent") relieved of their menopausal and articular symptoms; 70 per cent responded in "striking and often dramatic fashion, obtaining almost complete relief." Including those "inadequately treated" 66 per cent of the total 53 patients were "helped" by estrogenic therapy.

2. "Menopausal atrophic and hypertrophic arthritis." Hall also noted 18 "castrates" who were well until castration and then, coincident with the onset of menopausal symptoms, developed unquestioned atrophic or hypertrophic arthritis as well as "arthralgia." "Because of the history, because no other cause could be found for the arthritis, and because the menopausal symptoms and arthralgias yielded to estrogenic therapy, one is tempted to conclude that castration or the removal of the internal secretions of the ovaries may be a direct or indirect cause of true arthritis. No such conclusion can be drawn on the evidence so far collected."

The studies of Gardner and Pfeiffer are of interest in this connection. Mice were injected weekly with comparatively large amounts (100 to 1000 international units) of estrogen (hydroxy-estrin benzoate) over long periods of time up to 348 days. There occurred an extensive resorption of parts of the pubic and ischial bones, and replacement of the pubic symphysis by an interpubic ligament; but elsewhere there was marked condensation of bone and replacement of marrow cavities with endosteal bone.

3. "Villous or climacteric arthritis." Current descriptions of this supposed entity continued to vary somewhat.[583, 723, 808, 917, 954] Its proponents consider it to be a distinctive clinical and pathologic syndrome; it is *not* atrophic or hypertrophic arthritis at the menopause. The French call it "lipoarthrite seche." It almost exclusively affects the knees of women (usually obese) at or near their natural or artificial menopause (Stone). According to others it may also affect other weight-bearing joints (hips, ankles—Robinson), the back (Oldershaw), occasionally wrists and thumbs (Thomson). Symptoms are aching stiffness of joints, mostly of knees, relieved by rest. Tenderness is confined to the involved parts of synovial membrane and is found mostly at the inner aspect of knees at the attachment of the internal lateral ligament to the internal femoral condyle.[583, 917] Pain and tenderness are "less severe than in atrophic arthritis." There is some "swelling" generally at the inner side of the knee joint. This swelling is due to periarticular fat pads, and to the enlarged synovia.[808, 917] Synovial effusion is not present according to Stone, but according to Robinson it is sometimes present due to trauma from pinching of the swollen synovial villi. According to Stone there is no restriction of articular motion; indeed mobility may be abnormally increased due to laxity of ligaments. But according

to Little joints are enlarged, tender and limited in motion in severe cases, but the periarticular changes and limited motion are never as severe in this disease as they are in atrophic arthritis. Common associated conditions are obesity and flat feet.

Roentgenograms of knee joints are negative except for the appearance of "small punched out areas behind the articular cartilage" with some bony decalcification from disuse, according to Little; they are negative in early stages, but may reveal secondary hypertrophic arthritis later in the disease, according to others.[808, 917] Robinson stated that "clinically and radiologically menopausal arthritis is identical with osteoarthritis," yet he insisted that it must be carefully differentiated therefrom.

[He did not clearly show how this could be done.—Ed.]

The distinctive articular pathology of villous arthritis was again said to be a "peculiar hypertrophic change" in synovial membrane (Thomson) with production of villous hypertrophy extensive enough to be palpable in severe cases (Little). There is no true arthritis, according to Stone; there is synovial hyperemia but no inflammation of the membrane. The fatty synovial fringes and villi increase in size and number, sometimes to the extent that the joint is packed with fatty arborescent growths, the branched villous processes insinuating themselves between patella and condyles and between condyles and semilunar cartilages with resultant pinching thereof. Fat in the posterior pouch of the knee is also increased (Stone).

[None of these writers presented photomicrographs of these pathologic reactions; they apparently relied on the published descriptions of others. If they have original material, it would be very helpful if they published it. We know of no one, certainly not in recent years, who has presented photomicrographic evidence clearly showing the pathologic specificity of villous arthritis with its differentiation from atrophic, hypertrophic and other common arthritides. No such entity is described in the standard works on articular pathology (Strangeways, 1905 et seq.; Nichols and Richardson, 1909; Pommer, 1913; Knaggs, 1926; Allison and Ghormley, 1931). The chronic villous polyarthritis of Schüller was classified by Stockman, 1920, under chronic infectious arthritis, in contrast to rheumatoid arthritis. We would appreciate receiving original references on the pathology of menopausal villous arthritis.—Ed.]

Etiology. The cause of the disease was variously considered to be a thyroid deficiency occurring at the menopause (Stone), primarily metabolic changes including thyroid deficiency, secondarily trauma (Thomson), a temporary ovarian insufficiency (Oldershaw). But no data concerning metabolic rates or hormone assays were given.

Treatment. Remedies recommended were reduction of obesity, mild hyperpyrexia with foam baths "to start weight reduction" (Stone), thyroid extract—"the sheet-anchor of treatment" used not only for its weight reducing effect but as replacement therapy (Stone; Thomson), rest and heat for affected joints ("exercise is bad" for these joints), use of a device to limit articular motion to prevent trauma to hypertrophied villi (Little), weekly injections of estrogenic material, faradic current to increase muscle tone even though the patient is resting, hydrotherapy "to increase metabolic

activity" (Thomson). Little performed synovectomy in intractable cases: "it may give relief for years"; in old severe cases he considered arthrodesis sometimes necessary. Oldershaw and Robinson used intrapelvic diathermy "to accelerate the endocrine activity of the ovaries." [No hormone assays were made to support this statement.—Ed.] Such treatments presumably arrested the arthritis in a relatively short time. If the disease is left untreated "osteoarthritis inevitably supervenes after a number of years. But here at least is one variety of preventable osteoarthritis; if treatment is undertaken thoroughly, most of these 'menopausal knees' get well" (Stone).

A general discussion of the use of estrin in the treatment of "chronic rheumatism" was given by Cawadias.

4. "Menopausal fibrositis." This was said to affect obese women at the menopause with signs of hypothyroidism. Reported features were mild myxedema, variously situated subcutaneous fat pads, and subcutaneous nodules which are sometimes very painful and tender but which on excision reveal only simple lipomas without signs of inflammation. Robinson used diathermy and deep massage to the nodules, and intrapelvic diathermy twice a week for one or two months; he stated that most cases were relieved thereby.

[No pathologic or biochemical studies were given to support these statements. —Ed.]

Juvenile Hip Disease from Hypothyroidism. A disturbance of ossification of the capital epiphysis of the femur in hypothyroid children was described by Benjamin and Miller. Two types of maldevelopment may arise: (1) one involving the epiphyseal plate may produce epiphyseal slipping; (2) the other produces osteochondrosis of the femoral head. Coxa vara may develop later.

Joints and the Parathyroids. Diseases of the parathyroids produce no known articular disease. Degenerative muscular lesions but no articular changes were noted by Cantarow, Steward and Housel in dogs with experimental acute hyperparathyroidism. Many patients with hyperparathyroidism, however, experience skeletal aches and pains which they call "rheumatism." The pain is usually localized to muscles and bones but sometimes to joints. In recent cases patients experienced "pains in arms and knees," [297] tingling pain in hands and feet, stiffness in legs,[608] pain and lameness in a hip,[345] stiffness, pain and aching in extremities,[900] weakness, fatigability, muscular hypotonicity and ligamentous relaxation.[901] Diagnosis becomes clear when the proper biochemical and roentgenologic studies are made.[327, 362, 496, 1003] The disease should not be confused with arthritis.

Miscellaneous Diseases of Joints

Pharmaceutic Arthralgia: "Chemical Arthritis." While taking certain drugs (e.g., thyroid extract, excess amounts of soda bicarbonate, bismuth) patients may note pain in muscles or joints sometimes called myalgia or

arthralgia medicamentosa, medicinal arthralgia, "paratherapeutic articular disturbance."[4] To this list O'Connor added lead, arsenic, radium and insulin (a biologic product, not a drug) as occasional causes of "toxic arthritis."

[No true arthritis occurs.—Ed.]

Intermittent Hydrarthrosis. Prolonged remissions of this disease may occur spontaneously, as a result of certain remedies, or during certain conditions such as pregnancy. Marked relief during pregnancy was noted by Hench in one case and he cited other cases previously reported. Swett advised synovectomy for the disease.

Synovitis. A patient with mild acute traumatic synovitis later slowly developed what Swett called "synovitis ossificans." Roentgenograms revealed extensive infiltration of synovia with actual bone. The membrane was removed, its pathology described.

Synovioma. This is a rare condition.[5] Clinical and pathologic data in a new case were reported. The swelling was behind the knee of a young man. After amputation of the leg the patient responded well.[166]

Synovial (Baker's) Cyst of the Knee: Posterior Synovial Herniation. Any cystic swelling about the knee in which the cyst has a cellular lining which simulates synovial membrane is a Baker's (1877, 1885) cyst. To be distinguished are a synovial "cyst" in the popliteal region resulting from posterior herniation of the synovial membrane of the knee joint, and the swelling caused by hyperplasia and inflammation of one of the posterior bursae of the knee. Synovial cysts from posterior herniation of the knee joint originate beneath the medial head of the gastrocnemius muscle where there is a natural weakness in the posterior capsule of the knee joint. Usually the greater part of the swelling is distal to the transverse flexion crease on the skin. These cysts are most noticeable when the leg is extended; they are not especially tender, but may produce aching, sometimes severe sharp pain and occasionally intermittent effusion into the knee. There may be considerable interchange of fluid between the hernial sac and the knee, hence the effusions in each may vary in size. Treatment is to remove the hernial sac surgically and repair the opening in the joint capsule. Results in 11 cases were reported (Edmunds and Hebble; Haggart).

Of the 12 bursae around the knee joint two are placed posteriorly and one is between each head of the gastrocnemius muscle and the joint capsule. The one beneath the inner head of the gastrocnemius extends between this muscle and the semimembranosus muscle and is called the semimembranosus bursa. Either of these posterior bursae may be connected with the synovial cavity of the knee. If they are not, the effusion of a bursitis cannot be pressed anteriorly into the knee joint. If they are connected differentiation between bursitis and posterior synovial hernia is more difficult.[401]

Tenosynovitis. Gould cited the common types, "simple tenosynovitis," the infectious forms including gonorrheal and tuberculous, and stenosing tendovaginitis, and ganglion. There are two types of stenosing tendo-

vaginitis: (1) a strictly local thickening of a tendon sheath of a finger flexor opposite a metacarpophalangeal joint causing a "snap-finger"; it is treated by surgical removal of the local fibrosis; (2) stenosing tendovaginitis at the radial styloid process (deQuervain's disease). As a result of acute or chronic trauma there is chronic thickening of the sheaths of the extensor pollicis brevis and abductor pollicis longus. There may be much tenderness over the radial styloid process and an elongated swelling from hypertrophy of the annular ligament. About 250 cases have been described, mostly in women. Ten new cases were reported (Cotton, Morrison and Bradford; Keyes). Palliative treatment should be tried but is "mostly disappointing" (Gould). Operative treatment is simple and satisfactory, often dramatically so.

Tenosynovitis Crepitans; Crepitating Peritendinitis. Howard's summary of 32 cases was reported in our last Review. He has now studied 72 cases. Chiefly affected were the extensor muscles of wrist and thumb. The disease may be caused by trauma or by functional overactivity. Its clinical and pathologic features were again described. Massage, baking and diathermy are contraindicated. Treatment involves absolute rest in plaster splints. Duration of disability with adequate immobilization was 12 days, with partial immobilization 23 days.

Ganglion. Simple ganglion is usually a swelling resulting from the mucinous degeneration of a fibrotic change in a small portion of the wall of a tendon sheath.[378] It is annoying but rarely disabling. Its contents can rarely be aspirated. Treatment involves pressure dispersion or incision (technic given) but not dissection except in special cases.

Osteochondritis. Legg-Perthes' disease has been called "osteochondritis deformans juvenilis" of the hip. It was described by Legg and Waldenström (1909), later by Calve (1910) and Perthes. The cause is unknown. Waldenström preferred the term "coxa plana" and described the changes in serial roentgenograms made in four early cases. Conservative and not surgical treatment was advised. To the five cases previously reported Goldenberg added a sixth case in which Perthes' disease followed traumatic dislocation of the hip. Changes radiologically similar to Legg-Perthes' disease but pathologically different may affect the hips of juvenile cretins as a result of imperfect ossification secondary to hypothyroidism. Five cases were reported (Benjamin and Miller; Albright).

Five new cases of juvenile ischiopubic osteochondritis were also reported (Corper; McFadden).

Arthropathy. The more common forms of arthropathy were listed by Worster-Drought thus: (1) tabetic arthropathy (Charcot's disease) including the rare form, tabetic vertebral osteo-arthropathy; cases involving a knee, a wrist and a metacarpophalangeal joint were reported [792, 1050]; (2) arthropathy of syringomyelia; a case involving both wrists was reported, also two cases of Morvan's type of syringomyelic arthropathy (atrophy and disappearance of terminal phalanges of fingers) in one of which there were ex-

tensive changes in a shoulder [613, 1050]; (3) posthemiplegic arthropathy, first described by Alison (1847), usually affects a shoulder; (4) hypertrophic osteo-arthropathy. Most of the cases of the last type are related to chronic pulmonary disease, others to congenital and valvular heart disease and less often to chronic hepatitis or enteritis. No primary lesion is discovered in lungs or elsewhere in from 4 to 14 per cent of cases (Locke, 1915). One case secondary to pulmonary new growth was reported.[1050] In one case, reported in much detail, no primary cause was found (Campbell, Sacasa, Camp). A case of clubbed fingers and toes associated with a congenital pulmonary cyst was also noted.[675]

Idiopathic Familial Generalized Osteophytosis. This condition somewhat resembles either atypical acromegaly or hypertrophic osteo-arthropathy but is considered different from either. Also called " familial acromegalic-like skeletal disease " its features are onset of the disease at puberty, progression by exacerbations, marked chronicity, extreme bony change, absence of known primary disease, and the presence of a familial tendency. Freund reported a case in which the disease started as a hyperplastic process of several joints and simulated subacute recurring arthritis.

Sclerodactylia. Features of this condition are stiffness, atrophy, and deformity of fingers with tightening, ulceration and pigmentation of skin. Roentgenograms usually reveal phalangeal decalcification, resorption of phalanges at the finger tips, amorphous, calcareous granules in phalangeal soft tissues, interosseous calcareous nodules, and various arthritic changes, mainly atrophic. Two cases presumably related to scleroderma were described.[376, 456] Also reported was a most unusual case of progressive diffuse scleroderma with sclerodactylia and calcinosis in a child aged 12 years, sick for 10 years, and now looking like no human being, as the photographs show (Pachman).

Hereditary Arthrodysplasia. Sever reported a case of this condition best described by Turner (1933). Its features were: patellae placed not in the usual position but on the external aspect of both knees, limitation of supination of hands and of extension and flexion of both elbows, rudimentary thumb nails, other nails being normal. Roentgenograms revealed the lateral position of the patellae with newly formed, articular facets on the lateral condyle of the femurs, and at elbows multiple exostoses. Hereditary arthrodysplasia apparently is seen only with hereditary dystrophy of nails. Several of the patient's relatives had the latter but not the former. The condition, inherited and congenital, apparently is due to some defect in the closing or fusing of the ectodermal and mesodermal layers of the embryo.

Arthrokatadysis: "Otto Pelvis." This is an intrapelvic protrusion, a sinking in or subsidence of the acetabulum with protrusion of the femoral head through it, resulting in limitation of motion of the hip. Wardell saw the condition in one hip of a woman with atrophic polyarthritis who had fallen on her hip. A Smith-Petersen acetabuloplasty gave satisfactory results.

Ehlers-Danlos' Syndrome. Four cases were described.[100, 788, 883,1010] Features were marked hypermobility of joints, excessive elasticity of skin, friability of skin and blood vessels, pseudotumors in the scars of lesions resulting therefrom, movable nontender subcutaneous spherules of fat in various regions.

Deposits of Calcium or Bone About Joints. It is often difficult to determine from roentgenograms whether these deposits are in tendons, ligaments, or bursae adjacent to joints. Milch and Green described several cases of calcification about the flexor carpi ulnaris tendon, with acute sharply localized pain and tenderness over the area around the pisiform bone, limited wrist motion, sometimes acute inflammation, and early subsidence of symptoms with the use of heat, immobilization and salicylates. It may be due to trauma. The deposits seemed to be in the tendon and not in peritendinous soft tissue or in the bursa subjacent to the flexor carpi ulnaris. Some of them disappeared under treatment. Buxton described "ossification" in the ligaments of the elbow from injury. One end of the ligament is torn from the bone and carries with it some periosteum; a hematoma results and bone cells are activated. Such a condition can be prevented by proper immobilization of the elbow after injury. Complete or partial absorption of deposits of bone in muscle may result from immobilization but as a rule "once bone is formed in ligament, it remains unchanged," probably because ligaments are too avascular to carry out the process of absorption.

[The writer spoke of "ossification" and deposits of bone, but no histologic evidence was given to indicate whether the deposits were of calcium salts (which may be rapidly reabsorbed) or true bone. One of us, A. J. K., believes they are true bone. —Ed.]

Brodie's Abscess Producing Chronic Arthritis. A boy with a swollen wrist was seen by Ray. The cause of the arthritis was an adjacent Brodie's abscess, a localized form of osteomyelitis.

Cartilaginous Changes Due to Rickets. Three cases of severe late rickets were studied at autopsy by Freund. Cartilage changes included edema and decomposition of hyaline ground substance, lack of cartilage calcification and enchondral ossification.

Diseases of Bursae

Meyerding noted the common types and the surgical treatment of bursitis: traumatic bursitis from acute but more commonly from chronic trauma (e.g., "miner's elbow"—olecranon bursitis; "coachman's bursa" or "weaver's bottom"—ischeal bursitis; "tennis elbow"—radiohumeral bursitis; "housemaid's knee," "nun's knee"—prepatellar bursitis), bursitis from nonspecific (rheumatic) or specific infections (e.g., tuberculous, syphilitic), and gouty bursitis. Commonest of all is the bursitis involved in a "bunion." Bursitis may occur not only in preformed bursae but also in newly formed bursae near bony prominences subject to injury.

Acute Hematogenous Bursitis. This condition may (rarely) arise in association with acute infections, septicemia, etc., and may cause chills, fever, prostration, and localized pain and swelling which may be mistaken for acute arthritis. Cooperman reported six cases: a subacromial bursa was affected in four cases; a gluteal in one and a prepatellar in one case. Diagnostic needling revealed pus and was followed by incision and drainage. Gluteal bursitis is often not diagnosed because it is difficult to know whether the hip joint or one of the 10 to 30 bursae in the buttock is affected.

Popliteal Bursitis. Already mentioned was posterior hernia of the synovia into the popliteal space which Haggart called "Baker's cysts," and its relationship to true bursal swellings from popliteal bursitis which Wilson, Eyre-Brook and Francis also spoke of as "popliteal cysts, Baker's cysts." [Obviously the term "Baker's cysts" has a different meaning for different writers. —Ed.] Wilson and his colleagues noted six primary bursae around the popliteal fossa and medial side of the knee, chief of which was the gastrocnemio-semimembranosus bursa. Its two parts are generally connected, hence the name. It frequently connects with the knee joint. Twenty-one popliteal cysts were removed at operation; most, if not all, of them were from fluid distention of the gastrocnemio-semimembranosus bursa, rather than synovial herniation. Although these cysts usually are connected with the knee joint (air injected into them passes promptly to the knee, as shown in roentgenograms), they usually remain distended despite attempts to empty their contents into the knee by pressure. This behavior suggests a valvelike action at the mouth of the cyst. It was believed that such cysts arise, not from infections or toxins but from injury to the bursal wall caused by single violent or repeated vigorous contractions of muscle which are followed by effusion. Operative excision was recommended: the cyst walls show blood pigment, fibrous thickening and cartilaginous and osteoid metaplasia.

Iliopectineal Bursitis. The iliopectineal bursa often connects with the hip joint. Inflammation of this bursa which occurs not infrequently, generally from trauma, is often undiagnosed. Finder reviewed the subject. Conservative treatment includes rest in bed and hot or cold compresses; aspiration will not cure the condition. Surgical excision, a tedious procedure, usually is recommended but Finder successfully treated a patient by surgical obliteration (closing the passage between bursa and hip, everting the walls of the sac and anchoring adjacent muscle fibers into its floor).

Calcification of Epicondylar Bursa. Hamilton saw a patient who clinically had severe "tennis-elbow": swelling, tenderness and heat about the external epicondyle of the humerus. In roentgenograms deposits of calcium on the radial side of the elbow were placed too laterally to be in the radial collateral ligament. Because the deposit of calcium was sharply defined and globular, it was thought to be in the bursa. A plaster splint was applied, later a cock-up splint. A month later symptoms and most of the calcium had disappeared.

"Subdeltoid and Subacromial Bursitis." These will be discussed under the next heading.

Diseases about the Shoulder Joint: "The Painful Shoulder"

Painful shoulders with varying degrees of stiffness are common. Some physicians blame them all on "subdeltoid bursitis"; others use the term "supraspinatus tendinitis" as their uniform diagnosis. Others realize that anatomically the shoulder joint is, like the back, a rather complex affair, and that like backache, a painful shoulder may result from a number of rather closely related and often overlapping syndromes. Each of these syndromes produces a somewhat similar symptom complex but each has its own distinguishing features. Various names have been given these syndromes: subdeltoid bursitis, subacromial bursitis, calcareous subdeltoid or subacromial bursitis, degenerating, calcified or ruptured supraspinatus tendinitis, Codman's syndrome, peritendinitis calcarea, scapulohumeral periarthritis, Duplay's disease, "shoulder joint complex," "painful shoulder syndrome," "frozen shoulder," periarticular fibrositis, periarthritis or "arthritis" of the shoulder joint. Some of these terms are synonymous but others are not. The different conditions may arise independently but more often they occur in definite relationship to each other. The structures involved, capsule, tendons and bursae of the shoulder, are so contiguous and functionally interdependent that disease in one may cause disease in another (Ferguson; Gray; Watson-Jones).

According to Codman (1934) "the subacromial, subdeltoid and subcoracoid bursa are one and the same thing, although films of tissue may separate them," depending on the anatomic position and also whether the arm is in abduction or rotation. The subacromial bursa (Codman's preferred term) has the deltoid muscle above it; its floor is formed by the fibrous tissue sheet composed of the fused tendons of the supraspinatus, infraspinatus, teres minor and subscapularis. Disease in these structures results sometimes from infection but more often from acute and chronic trauma.[81, 279, 819, 827] The bursa may be affected primarily, but is more often affected secondarily from disease in the musculotendinous cuff (especially the supraspinatus tendon and muscle) or in the bones of the shoulder joint. The deposits of calcium near the bursa were first thought to be within the bursa (Painter, 1907). It is now believed that they are usually not inside the bursal sac, not even within its walls, but in the region just beneath the bursa, generally in the tendon of the supraspinatus muscle near its insertion but sometimes in the tendon of the infraspinatus, subscapularis or teres minor.[279, 662, 819, 827] When deposits of calcium are present within the bursa they generally have ruptured into it from the underlying tendon (Rubert).

1. Supraspinatus Tendinitis without Calcification. The supraspinatus muscle and tendon are common sites of disease because the muscle is weak; its progenitor was designed to work with the force of gravity and swing the foreleg of quadrupeds

but in its human form it must work against gravity to raise the arm; it is attached close to the fulcrum of a long lever, and it can be pinched easily between the humerus and the acromion (Ellis). Being relatively avascular, the tendon commonly degenerates; an attrition lesion results from the metabolic change of age and trauma.[819] Symptoms of degenerative tendinitis include painful but not limited abduction with maximal tenderness at the greater tuberosity of the humerus where the tendon is inserted. Pain is most notable when the arm is being moved in abduction through the part of the arc between 60 and 120°. During this part of the arc the tendon impinges against the acromion process; abduction of more than 120° is painless as the tendon slips under the acromion process and there is no impingement or strain.[1006] Treatments used include diathermy, radiant heat or injections of 5 to 10 c.c. of 2 per cent procaine which may give great relief for five or six hours, sometimes much longer (Watson-Jones).

2. Supraspinatus Tendinitis with Calcification. Acute trauma may cause a muscle bruise with effusion of blood, a tear in some fibers of the tendon, or partial evulsion at its insertion. The blood in the hematoma is altered into an amorphous calcareous mass (calcium phosphate and carbonate) deposited "wholly within the tendon"[1006] under the bursal floor.[279] Thus the deposits of calcium in cases of "subacromial bursitis" result from slight tears in the supraspinatus tendon which nature has attempted to repair (Codman 1934; Outland and Shepherd). How often degeneration of the muscles and tendon precedes and predisposes to tears and how often the tears precede and cause localized degeneration is undetermined. The symptoms of supraspinatus tendinitis with and without calcification are about the same except for roentgenographic evidence of changes in the former. In acute cases pain and disability may be great.

Deposits in the supraspinatus tendon were compared to those occasionally seen in other tendons, e.g., about the wrist, elbow, knee or hip. In all these cases the same basic lesion and symptoms were present. Hence for them Sandström and Howard proposed the general term "peritendinitis calcarea." Among 320 cases studied by Sandström deposits were at shoulders in 259, hips in 48, elbows in 6, fingers in 6, knees in 5, toes in 3, wrists in 2 cases [a total of 329 cases as some patients had more than one deposit.—Ed.] Fever occurred in 70 of 80 cases in which temperature was taken; sedimentation rates were elevated in 70 of 75 cases. The disease occurred any time after the age of 10 years, but most often after the age of 40 or 50 years. In these 320 cases the calcium was partly in tendons, tendinous, capsular and ligamentous tissues, partly in periarticular and peritendinous connective tissue, only once in the wall of a bursa and never within a bursal sac. Additional pathologic reactions were necrotic changes in tendons, ligaments and joint capsules, marked vascular changes (hypertrophy of the media), and some regenerative processes. According to some[1006] the tooth-paste-like deposits of calcium may induce a secondary irritative hyperemia which may cause spontaneous resorption of the calcium and may also cure the underlying tendinitis. But deposits should not be removed surgically simply because they are present. The pain is due, not necessarily to the deposits of calcium, but to the lesions which foster them. In some cases an opposite symptomless shoulder may show as much or more deposit of calcium than the painful one. The deposits often disappear spontaneously, sometimes within a few days, or they may persist despite treatment which relieves all other signs and symptoms.

Conservative treatment, such as various types of physical therapy and rest, should be used first.[81, 819] Martucci preferred to use diathermy daily with the arm in a sling night and day for about two weeks; then massage and high frequency currents. The joint should not be fixed in plaster or it may "freeze." Some advised the use of an abduction splint.[81, 279] New abduction splints were described (Bettmann); particularly ingenious was that of Papurt in which a light leather cap is fitted with a ring and a wrist bracelet with a snap. The wrist is merely snapped to the cap after

it is on the head, and thus abduction is maintained. According to Watson-Jones in many such cases the shoulders cannot be supported in abduction as they are too painful. Acute pain may be relieved by injections of 20 c.c. of 1 per cent solution of procaine into and around the bursa.[81,662] For small deposits, diathermy, radiant heat and massage generally suffice. Troedsson noted disappearance of deposits in 13 of 30 cases after 6 to 45 hours of diathermy given within 3 to 11 weeks by a technic which he considered superior to others. Sandström considered roentgen therapy most satisfactory in both acute and chronic cases (technic given). Deposits of calcium often disappeared after two or three weeks, sometimes longer. Treatment for several months was necessary in some cases and deposits did not always disappear completely. [But many roentgenograms were published showing the disappearance of the deposits.—Ed.] Surgical evacuation of the deposits is necessary in some severe cases and may give immediate and complete relief (Watson-Jones). Meyerding recommended operation only if the deposits were associated with pain and other symptoms, and if conservative therapy was unsatisfactory. Manipulation of such painful stiff shoulders under anesthesia is sometimes successful but should be done with great care; Meyerding described the technic.

3. Rupture of the Supraspinatus Tendon (Complete or Incomplete). When degeneration of the muscle and tendon has resulted from age and chronic trauma, very slight acute trauma is needed to injure them even further. Hence partial or complete rupture of the tendon is common among elderly people and those in certain occupations (painters, plasterers). It is found in from 17 to 30 per cent of cadavers (Keyes, 1935; Watson-Jones) and is considered by some [279] the commonest cause of painful shoulders among industrial workers. When the tendon is torn, the floor of the subacromial bursa is sometimes, but not always, torn with it, creating an opening between the bursa and the shoulder joint.[741] Symptoms and signs of incomplete tendinous rupture are rather similar to those of tendinitis: pain in the shoulder, sometimes referred to the insertion of the deltoid, tenderness at the greater tuberosity of the humerus, limited and painful internal rotation, abduction between 70 and 90° which is probably possible but very painful and associated with the characteristic "catch" of pain as the injured fibers pass the acromion.[1006] According to Ellis a partial rupture almost always heals but it may take six months. Treatment by heat and gentle motion was used; Ellis used a sling; others advised immobilization in abduction and external rotation for from three to six or eight weeks and surgical repair thereafter if relief is unsatisfactory.

Clinical signs of complete rupture include sudden onset of sharp pain, loss of power to abduct the arm, tenderness over the greater tuberosity [741] or at the tip and lateral aspect of the acromion [279] (some found Dawbarn's sign not very helpful),[741] undue prominence of the greater tuberosity because its tendinous covering is absent, a fine crepitus on palpation of the tuberosity as it moves under the acromion on passive motion of the arm. The "diagnostic sign" of the condition, according to Watson-Jones, is greater limitation of active than of passive abduction in the presence of a normally contracting deltoid. Weak abduction to about 60° is possible but no more; there is no true glenohumeral abduction. Conservative treatment involves immobilization of the shoulder with the arm at 90° abduction and 60° external rotation for 8 to 10 weeks by the use of a frame and meanwhile active exercise for fingers, wrists and elbows.[1006] According to some the opening between the subacromial bursa and the shoulder joint will never heal and must be repaired surgically. The technic was described.[279] Of 12 patients so treated four had excellent results, four good, three fair and one poor (Outland and Shepherd).

Partial or complete rupture of a supraspinatus tendon may cause secondary effects in adjacent tissues: chronic subacromial bursitis, eburnation and rounding off of the greater tuberosity, degeneration, fraying and eventual rupture of the long head of the biceps, excrescences and osteophytes along the edge of the acromion and the tip

of the greater tuberosity, slight erosion of articular cartilages of the shoulder joint (Ferguson).

4. Subacromial (Subdeltoid) Bursitis (with and without Calcification). Four types of bursitis were again listed by Ferguson (features of which were noted in our last Review): acute traumatic bursitis without calcification, acute bursitis with calcification, chronic bursitis with or without calcification and chronic adhesive or obliterative bursitis. The last was characterized by atrophy of shoulder muscles and very limited motion of joint and was called the "frozen shoulder" (a term which others reserved for a condition to be described hereafter). Cases of simple subacromial bursitis are rare[1006]; usually bursitis and tendinitis with or without deposits of calcium *beneath* the bursa are present. Occasionally infection but usually trauma was considered the cause.[203] Symptoms are about the same as those of tendinitis. In Collins' experience the pain was usually greater at night and was most severe at the insertion of the deltoid and "seldom over the region of the bursa." Among Rubert's 288 cases of "subdeltoid bursitis" there were pain and limited motion in 95 per cent, a tender point over the greater tuberosity in 58 per cent, muscle atrophy in 20 per cent, atrophy of the head of the humerus in 22 per cent, associated arthritis in 16 per cent, calcification in the region of the bursa in 18 per cent. In 15 per cent pain extended to the deltoid insertion and sometimes to the neck and down the arm to the wrist.

In acute cases rest, heat and morphine are required. Injection of 15 to 20 c.c. of 1 or 2 per cent solution of procaine into the bursa and the capsule of the shoulder joint was recommended.[203, 471] In 18 cases the average disability after such treatment was 4.7 days.[471] Injections of 500 c.c. or more of "normal saline" solution were used by some[203] to distend and rupture the painful sac. Spontaneous recovery often occurs. If conservative therapy fails, the bursa should be explored and the deposits of calcium and thickened fringes removed (technic given).[203] In 147 of Rubert's 168 cases conservative treatment was used; results were good in 69 per cent, moderate in 19 per cent, poor in 12 per cent; in those cases in which surgical treatment was employed results were good in 48 per cent, moderate in 24 per cent, poor in 28 per cent.

5. "Periarthritis of the Shoulder": "Scapulohumeral Periarthritis." This was described by Duplay in 1872, but the term "periarthritis humeroscapularis" is considered poor by some.[81] Other names are Duplay's syndrome, and scapulohumeral fibrositis. The condition results from trauma or from "rheumatic fibrositis."[1006] It may be closely related to the syndromes already described in this section: in one of Duplay's cases which came to necropsy the inflammation apparently had spread from a subacromial bursa to neighboring structures. Among Douthwaite's 37 cases the main causative factor was trauma in 12, fibrositis in 14, unknown in 10; in one case the condition came on after hemiplegia. The condition was on the right in 21, left in 15, bilateral once. Symptoms arise spontaneously or after trivial trauma. The joint is not swollen. Pain is *not* confined to the greater tuberosity or region of the supraspinatus but is diffused and there are many tender spots. Internal rotation and forward and backward flexion may be free but abduction and external rotation are limited first by muscle spasms, then by adhesions about the whole joint capsule, "the frozen shoulder." Roentgenograms generally do not indicate any abnormality.[252, 1006] For the acute stage rest with the arm in abduction, heat, massage and hydrotherapy especially were recommended[211]; injections of procaine hydrochloride were less helpful than in other conditions.[471] "Most important" is active exercise ten minutes every hour of the day and the "worst treatment" is manipulation of the shoulder under anesthesia. The latter increases the serofibrinous exudate (Watson-Jones). Others,[302] however, favored such manipulation; results were excellent in 95 per cent of Douthwaite's cases. Dilaudid was used for severe "post-manipulation pain."

6. Fractures and Other Traumatic Lesions of the Shoulder. Fractures and dis-

locations of the shoulder may be associated, of course, with some of the aforementioned syndromes.[383,1006]

7. Tenosynovitis of the Long Head of the Biceps Brachii. According to Schrager this is a "new" entity described by F. Pasteur, 1932, unknown to American literature, but the commonest cause of shoulder pain. It may be caused by trauma or infection. In acute cases pain and disability are severe. Schrager tabulated the features distinguishing it from the other conditions just described. The most important diagnostic feature is tenderness and pain in the bicipital groove. The patient cannot raise the arm above the level of the shoulder (not even with assistance), nor can he abduct it or place the dorsum of the hand against the back. In acute cases treatment consists of morphine, rest in bed, support of the arm by pillows, and diathermy. Much benefit and occasionally "instant cures" can be obtained by sudden traction (rationale and technic given). In less acute cases diathermy, massage and exercises were used.

8. Calcification of the Bursa of the Coracoclavicular Ligament. This represents another possible cause for painful shoulders. In McCurrich's case, presumably the first one reported, pain and swelling below the outer part of a clavicle appeared some months after a fall on the shoulder. A large calcified deposit was found in the region of the coracoid process and excised. Its position was much more mesial than that of deposits previously mentioned.

9. Pulmonary Tumor Simulating Subacromial Bursitis. Symptoms characteristic of subacromial bursitis developed in one case. "Calcified subacromial bursa" was removed but symptoms persisted and later were found to be due to a slowly growing neoplasm of the apex of the lung, a superior pulmonary sulcus tumor (Nathanson, Hochberg and Perlman).

10. Shoulder Pain from Cervical Ribs. Stinchfield reminded us that symptoms resembling "arthritis" of the shoulder occasionally may result from such developmental anomalies as cervical ribs.

Diseases of Muscles and Fibrous Tissue

Classification. Bach divided diseases of muscles as follows: (1) diseases of muscles secondary to diseases of bones and joints, (2) primary diseases of muscles caused by (a) infective or toxic agents, (b) metabolic changes, (c) trauma, (d) mechanical or static agencies. His classification of "muscular rheumatism" follows:

I. Those essentially inflammatory and infective in origin.
- *A.* Diffuse septic myositis (i.e., metastatic abscesses).
- *B.* Dermatomyositis.
- *C.* Myositis ossificans.
- *D.* Myositis fibrosa.
- *E.* Myositis secondary to "focal infection."
- *F.* Muscle lesions of glanders.
- *G.* Muscle lesions of echinococcal infections.
- *H.* Muscle lesions of gonorrhea.
- *I.* Muscle lesions of syphilis.
- *J.* Muscle lesions of tuberculosis.
- *K.* Muscle lesions of typhoid fever ("Zenker's degeneration").
- *L.* Muscle lesions of scurvy (intramuscular hemorrhages, localized inflammation).
- *M.* Muscle lesions of hemophilia (hemorrhages, localized fibrosis).
- *N.* Muscle lesions of rheumatic fever.
- *O.* Muscle lesions of subacute bacterial endocarditis.

II. Those which are noninflammatory and usually not infective.
   A. Myalgia associated with other conditions.
      1. Extraneous physical causes, e.g., chilling ("fibrositis," "myogeloses").
      2. Fatigue, overexertion, acute trauma.
      3. Metabolic disturbances such as gout and high blood pressure.
      4. Drug therapy ("les rheumatismes de la chemotherapie"), e.g., arsenic, bismuth, mercury, gold, barbiturates, chloral, antipyrin, atophan.
      5. Chronic nervous exhaustion, inferiority complex, etc. (psychoneurotic rheumatism).
   B. Panniculitis.

Bach's descriptions of these types were too brief to be helpful in diagnosis. Bach and also Gutstein noted that obese women with high blood pressure often have vague rheumatic pains ("hochblutdruck-rheumatismus") in neck and shoulders, extending down the arms, sometimes also to the thighs. Concerning myalgia from chemotherapy Bach stated: "The clinical signs vary from transient muscle pain to hydrarthroses." Bach accepted Gower's view that despite specific differences the various forms of "chronic myositis" have a basic identical pathologic picture: an inflammatory reaction in connective tissues.

[This classification has certain inconsistencies, but is here given because of the rarity of such classifications.—Ed.]

Diseases of Muscles Caused by Trauma

A general discussion of the types and treatment of muscle injuries was given by Page.

Rupture of Biceps Brachii. Waugh stated that rupture of the biceps brachii occurs more frequently than is generally believed. He noted 14 cases among 28,755 cases admitted to two general hospitals. Causes of the conditions were indirect trauma in seven, direct trauma in four, stabbing in one, unknown in two cases. The long head and its tendon were affected in 12, the "lower" tendon in two cases. Including the latter, 25 cases of ruptured "lower" tendons have been reported in the literature. Symptoms and signs were discussed. The most constant sign was a deforming change in the contour of the muscle. Treatment should be conservative in cases of partial rupture or little disability. Surgical repair is indicated in others; it was done in 12 of the 14 cases.

Myositis Ossificans. Geschickter and Maseritz studied 25 cases of myositis ossificans, 23 of the circumscribed, 2 of the progressive type. The usual cause was trauma (in 60 per cent of the cases); sometimes the cause was unknown. Occupation played no rôle. The thigh was affected in 13 cases, the arm in five, elbow in two, lumbar region and neck in one each, multiple regions in one, and unstated regions in two. Pathologic reactions were described. Conservative treatment was recommended (no details given) since postoperative recurrences were common. In the four other cases reported involvement occurred in the biceps after injury to the elbow,

the anterior axillary fold after fracture of the humerus,[674] a tendo achilles after injury (16 such cases in the literature) [354] and in tissues in a suprapubic scar near the left pubic bone, involved after prostatectomy.[846] Only eight cases of postoperative myositis ossificans have been reported. Page noted that the disease may occur after the excessively tight application of a tourniquet. He advised complete rest of the affected part in a plaster cast for several weeks. Resorption of ectopic bone may occur. Surgical excision should be performed only in cases more than one year old that have limitation of motion in an adjacent joint.

Infectious Myositis

Three cases of nontuberculous iliopsoas abscess were reported, two from *Staphylococcus aureus* (Lewis), one from gram-positive diplococci in a case of pneumonia. In the latter bilateral psoas abscesses, the first on record (Ortmayer), were present.

Fibrositis

Most articles on fibrositis concern that type of unknown etiology which some call "primary fibrositis." When fibrositis appears as a recognized part of some definite general disease (e.g., rheumatic fever) it is (or should be) spoken of as "secondary fibrositis."

Primary Fibrositis. Clinical features. The disease is common among London busmen.[915] Its clinical features and the characteristic painful, aching stiffness it produces were again described.[377, 397, 525, 750] Comments were made on two anatomic types of fibrositis less well-known than others: spinal fibrositis and fibrositis of the abdominal wall. Patterson considered the latter more common than supposed (no details given). Gordon considered spinal fibrositis (acute and chronic lumbago) "the most important rheumatic affection of the spine." The frequent presence of tender spots with thickened bands, plaques and nodules was noted. Some of the indurations are tender, others are not. "Hence, while the presence of a thickening is a necessary prelude to an attack of fibrositis, acute or chronic, the thickening must, so to speak, be awakened into activity before the attack is precipitated."

The ameliorating effect of various types of jaundice in nine cases and of pregnancy in two cases of primary fibrositis was noted by Hench; its possible significance has already been discussed herein.

Laboratory data. Arneth counts were essentially normal.[357]

Pathology. No new data were offered. Writers continued to quote Stockman (1920) thereon. The fibrotic thickenings were interpreted as local tissue reactions to irritating deposits of some sort.[377]

Etiology and pathogenesis. The usual etiologic factors were mentioned: trauma, exposure to cold, "metabolic changes," influenza, tonsillitis and other infections.[135, 612, 750, 954] These are probably only predisposing and precipitating factors: the real cause is unknown. The assumption that the ir-

ritating material is necessarily of bacterial origin "has been all too hastily and uncritically accepted"; it is probably sometimes of bacterial, at other times of metabolic origin, perhaps related to accumulated muscle metabolites (Gordon). The similarity of fibrositic symptoms to the aching stiffness from muscle exertion is too close to be overlooked; the rôle of lactic acid and other muscle metabolites in this disease deserves reinvestigation (Patterson). Freund considered unproved the idea that fibrous tissues are predominantly affected in nonarticular rheumatism. "Fibrositis is certainly a misnomer and should be replaced by the term non-articular rheumatism, or even better, muscular rheumatism, if it could be proved that any rheumatic pain and stiffness are caused by pathological changes in certain muscles or tendons. . . . Whatever the primary cause and the contributing factors may be [the myalgic spot] is brought about by a temporary spasm in the capillaries leading after some time to a hardening of the muscles which might be described as congelation." Some writers suggested that the disease is related to an "imbalance of electrolytes," a disturbance in the calcium-potassium-sodium ratio of muscles.[335, 397, 750]

Treatment. Removal of infected foci was advised generally, but its results were often disappointing.[377, 531] Strapping and extra rest were used for acute localized fibrositis. Each form of physical therapy had its adherents: infra-red,[63, 64, 397] hot packs and douches,[377, 953, 954] brine baths[696]; ultraviolet irradiation seemed useful to some,[63] of little value to others.[377] "The sheet anchor of treatment is the right sort of massage together with sweating. Just any massage will not do" (Gordon). Muscles must be relaxed and the nodules must be kneaded against subjacent bone, sometimes a "very painful business." The skin should be "improved by a hardening process" (undescribed).[42] Intramuscular injections of oxygen or of procaine hydrochloride were recommended.[42] In his cases Kellgren noted wide areas of "referred pain and tenderness" associated with much smaller tender spots. The latter were considered the chief sites of disease since pressure thereon reproduced the patient's more diffuse complaints. Into these spots 5 to 70 c.c. of 1 per cent procaine were injected in eight cases of fibrositis of 2 to 52 weeks' duration. After a momentary exacerbation of the referred pain symptoms promptly disappeared. [The follow-up periods were usually only 1, never over 3 weeks.—Ed.] Excellent results presumably followed injections of sterile milk[612] or histamine.[254] Douthwaite[253] considered the use of iodine beneficial, gold salts "probably inadvisable." Injections of bee venom were considered useless by some,[254] useful by others[144]; Reichart injected it into the tender nodules and reported notable relief after 1 to 10 injections in some cases. The diet commonly used was to control obesity and constipation.[135, 377] Gutstein prescribed a salt-free, vegetarian diet to eliminate the sodium and increase the intake of potassium and calcium. By the use of this diet and other measures he "cured" 48 of 52 patients. Manipulation under anesthesia was recommended in cases of fibrositis of spine or shoulders with considerable stiffness.[377, 759]

Secondary fibrositis. Comments on the involvement of fibrous tissue in gonorrhea, in atrophic arthritis and in hypertrophic arthritis (" senescent fibrositis ") have already been made herein. Several writers discussed "gouty fibrositis." [136, 359, 449, 956]

Miscellaneous Diseases of Muscles

Psychoneurotic Rheumatism or Myalgia. Halliday extended his thesis (outlined in our last Review) that fibrositis is a definite entity but that many cases of so-called fibrositis really represent " psychoneurotic rheumatism."

If for any reason an emotional reaction is maintained for some time, illness may result. The emotional reaction may " emerge " into any one of several symptom-complexes including one somewhat resembling " fibrositis " or " rheumatism." Methods for carrying out the proper psychologic examination were described. Especially prone to psychoneurotic rheumatism are persons aged 35 to 45 years, widows and widowers, married persons who live apart, lonesome persons, miners, workers at heights (steel workers), clergymen, typists, housekeepers, nurses, pieceworkers, teachers, traveling salesmen, and " those in sheltered clerical occupations in which the instinct of creation is continuously thwarted." The condition commonly affects parts of the body previously injured or operated on. The complaints are often expressions of " symbolism." It is especially difficult to diagnose the condition and treat those persons in whom true fibrositis antedated or followed the onset of psychoneurotic rheumatism. Gutstein agreed that psychoneurotic rheumatism exists but considered it less common than suggested by Halliday.

Epidemic Myalgia or Pleurodynia. MacDonald again reviewed the studies made by himself and others on 70 children affected in a recent Cincinnati epidemic: these were noted in our last Review.

Dermatomyositis. An interesting case was seen by Lane: a young woman had an erythematous edematous rash three days after alveolectomy. Pains of joints and muscles and leukopenia developed. A diagnosis of lupus erythematosus disseminatus was entertained until muscle tenderness and edema developed. The diagnosis of dermatomyositis was confirmed by biopsy of muscle. A preëxisting carcinoma of breast was present. Postmortem findings were reported. The similarity of dermatomyositis and lupus erythematosus disseminatus was stressed, common symptoms being rash, edema, fever and pains of the joints. In the former leukopenia is rarely present and pain is more muscular; pain in joints and leukopenia characterize the latter.

" Muscular Rheumatism Associated with Spina Bifida Occulta." Dittrich attempted to show that " muscular rheumatism " even in the upper extremities is " invariably " caused by disturbances of sacral nerve roots associated with spina bifida occulta and that surgical correction of the spinal condition eliminates the muscular symptoms. Ten cases were described: their muscular pains and tenderness were mostly in the feet (usually with pes equinus) but also in thighs and low in back, occasionally in upper extremities. Tendon reflexes of knees and ankles were usually abnormal; constipation and colonic spasm were present. At operation the first, second and third

sacral laminae were removed, also deposits of "fibro-adipose tissue" overlying the dural sac and nerve roots. Thereafter muscle tenderness, pain and spasm were eliminated "in all cases." The mechanism of relief was admittedly not clear. Elimination of symptoms in muscles supplied by sacral nerves "would indicate a direct nerve effect" but the relief in other muscles and the improved intestinal tone suggested a systemic effect: perhaps an intestinal toxemia of etiologic importance was corrected.

[The writer's clinical description of "muscular rheumatism" is vague. His emphasis on the presence of pains of the feet and aching fatigue in muscles of legs and feet with deformities of the feet suggests that postural muscle fatigue was present and not true muscular rheumatism or "fibrositis." It is difficult to relate these symptoms to spina bifida occulta.—Ed.]

Miscellaneous Conditions

Aseptic Necrosis of Bone. Among 10 patients with aseptic necrosis of bone from arterial occlusion studied by Hirsch were four with chronic pain in joints adjacent to the affected bone; symptoms resembled "arthritis." The causes of the vascular constrictions or occlusions were not clear; trauma had occurred in seven cases. Inflammatory reaction and occlusion by fibroblastic tissue of affected vessels resulted in localized infarction of bone. Secondary articular changes were sometimes produced. If large enough, infarction of bone is evident in roentgenograms.

[Perhaps some such process is related to certain types of hypertrophic arthritis in hips with cystic regions in bone. Unfortunately no roentgenograms of joints in these cases were published.—Ed.]

Periarteritis Nodosa. Although still uncommon, this disease is not as rare as was once thought. Since first described by Kussmaul and Maier (1866) at least 395 cases have been reported; a clinical summary of them is being made (Boyd). It is a vascular disease of unknown origin. The lesions are so widely distributed throughout the body that a protean and often bizarre clinical picture is produced; hence until recently it usually has not been diagnosed before death. The clinical features are those of infection, and include irregular fever, sterile blood cultures, weakness, prostration in acute cases, cachexia, secondary anemia, leukocytosis, eosinophilia (up to 79 per cent of leukocytes) in 12 per cent of cases, in addition to the signs and symptoms from the vascular lesions in the various affected organs (heart, kidneys, lungs, appendix, gall-bladder, skin, etc.). It is often mistaken for "rheumatism" because of symptoms referable to nerves, muscles and joints. A true neuritis often occurs. The focal myositis produces muscle pain and tenderness which sometimes are worse at night. The fever and diffuse pain in muscles and joints may resemble "rheumatic fever." Eleven new cases were reported. In some of them symptoms included severe cramps in the legs, called "rheumatism" (Sandler), pain in extremities (Ashour; Berger and Weitz), pain in muscles and joints of extremities and true neuritis (Kernohan and Woltman). Vining's case was of special

interest. Initial symptoms included generalized pain, fever, muscle soreness and a red swollen wrist. The initial diagnosis was rheumatic fever. From time to time there was swelling of joints, presumably from periarticular nodular erythematous formations rather than from synovitis. Later arms were flexed and a shoulder was fixed and painful. A connection between periarteritis nodosa and rheumatic fever has been suggested.[190, 990] Among 100 unselected cases of the disease reviewed by Boyd were 34 with a history of rheumatic fever.

[One of us, M. H. D., recently saw a patient with marked articular changes and subcutaneous nodules resembling those of atrophic arthritis. Diagnosis of periarteritis nodosa was proved by autopsy. He also has seen two other patients with atrophic arthritis who later had periarteritis nodosum proved at autopsy.—Ed.]

Disseminated Lupus Erythematosus. Chief features of this disease are fever, articular symptoms, leukopenia and eruption on skin, later nephritis. The eruption on the skin often antedates the articular pain or the two may appear together. Occasionally the fever and pain antedate the eruptions; such cases resemble rheumatic fever somewhat.

A case was reported[165] in which symptoms included fatigue, loss of weight, cough, fever, sore muscles, attacks of hot swollen joints, persistent cutaneous lesions and hemorrhagic tendency. Splenectomy was done for "thrombocytopenic purpura." Severe recurrent polyarthritis, not just arthralgia, occurred; the leukocyte count was 4,000. Subsequently a diagnosis of lupus erythematosus disseminatus was made and proved at necropsy but in addition typical vascular lesions of periarteritis nodosa were present.

Arachnodactylia (Marfan's Syndrome, 1896). Features of this disease are abnormally long fingers and toes, decreased subcutaneous fat, generalized underdevelopment of muscles, ligamentous relaxation, sometimes bilateral dislocation of the lens with tremulous iris, deformities of joints, especially of feet with contractures, and certain other developmental defects. About 200 cases have been reported. Two more are described (Futcher and Southworth).

Calcification of Hyaline Cartilage. Cartilage from ribs, bronchi, trachea and larynx was obtained at autopsy from 97 men and 105 women. Falconer concluded that calcification of hyaline cartilage is common after 50 years of age. Cartilages of ribs of men are most often affected, those of trachea and bronchi of women.

Other Studies on Joints and Related Tissues

Articular Physiology. By a modification of methods used to isolate chondroitin-sulfuric acid from cartilage Meyer, Smyth and Dawson obtained from synovial fluid a sulfur-free and phosphorus-free polysaccharide apparently identical with hyaluronic acid, the polysaccharide isolated from bovine vitreous humor, human umbilical cord and hemolytic streptococci (Lancefield, Group A). Its presence in the latter seems significant in view

of the possible relationship of those bacteria to joint diseases. Iob and Swanson reported studies on extracellular and intracellular water in bone and cartilage. The proportionate distribution of mucin in 168 specimens of human synovial tissue from inflamed joints, tendovaginal coats and bursae, stained by Mayer's mucicarmine method, was studied by Cherry and Ghormley. It was concluded that synovial mucin results from cellular disintegration and not from a true secretion.

[One of us, W. B., does not agree.—Ed.]

A theory that an alternating ischemia and hyperemia, produced by the contraction and relaxation of muscles, maintains normal calcification of bone was presented by Blair. Hyperemia causes rarefaction, decalcification of bone and osteoporosis; a relative ischemia produces consolidation of bone (Grieg, 1931; Jones and Roberts, 1934). Maintain the circulation within certain limits and bones remain unchanged. If hyperemia produces resorption of bone, the use of heat in certain conditions (e.g., recent fractures) is wrong, according to Blair. Heat should be used only when it is desired to absorb calcium, as for example, in calcification of subdeltoid bursa or other heterogenous calcification [e.g., myositis ossificans. Some of us have found heat useless in myositis ossificans.—Ed.] " The use of heat in acute bone atrophy is a vicious practice, because it increases the pain and absorption of bone. Massage should also be used with discretion in the presence of atrophic bone as it too increases circulation. The value of contrast baths may be due to the fact that it produces an alteration of the blood supply to the part." In cases of bone atrophy of a part, as in fracture [or atrophic arthritis?—Ed.] Blair advised, on theoretical grounds only, the use of alternating suction and pressure to increase and diminish the blood supply.

[This paper is hypothetical but also thought provoking.—Ed.]

Additional papers of interest were those on the relation of cartilage to the repair of bone,[91] the effect of hypertrophic cartilage on growth of bone marrow,[475] the evolution of the knee joint,[440] and the morphogenesis of the architecture of the shoulder, hip and thigh.[472, 473]

Articular Roentgenography. Improvements in roentgenographic technic were reported. All roentgenograms of shoulders should be made with the patient upright, not lying down, for details of the joint are then more clear.[186] With Ottonellow's method the second cervical vertebra and those below it can be shown on one film.[487] A technic was devised to obtain better true lateral projections of the thoracic portion of the spine.[318] By taking anteroposterior views of clavicles with the patient *standing 72* inches from the tube both acromioclavicular joints can be visualized without distortion in one roentgenogram.[462] The little known technic of Gaenslen (1936) was considered best in obtaining lateral views of hips.[189]

Pneumoroentgenography of knees was considered simple, harmless and valuable in the diagnosis of internal derangements, osteochondritis dissecans, chronic villous synovitis, hypertrophied fat pads, Baker's cysts and loose bodies. Correct diagnoses as verified by arthrotomy, were made in 87 per

cent of one series,[784] in 97 per cent of another.[411] Injections of sterilized oil into joints for diagnostic purposes was considered useless, sometimes harmful.[495]

Articular Function. A small compact pendulum arthrometer useful for measuring improvement in joint motion was described.[418]

Experimental Arthritis. 1. Infectious. Certain hemolytic and green-producing streptococci, given intravenously to rabbits by Cecil and Angevine in single, much smaller doses than generally used, produced in many rabbits a *nonsuppurative* proliferative polyarthritis similar to, but admittedly not completely identical with, human atrophic arthritis. Streptococci disappeared from the blood stream within a few days after the injection and did not reappear. They were grown repeatedly from aspirated synovial fluid during the first week but rarely after three weeks even though articular changes persisted as long as 18 months.

[The large doses of bacteria previously used by most workers generally produced acute suppurative lesions and not *chronic* nonsuppurative polyarthritis. In this study one of the nearest approaches to the experimental production of a bacterial arthritis simulating human atrophic arthritis was made.—Ed.]

2. Chemical and nutritional. Extracts and implants of the anterior lobe of the pituitary given to guinea-pigs not only altered endochondral ossification but also produced degenerative and hypertrophic changes within the joints, chiefly swelling of the chondromucoid matrix, atrophy and degeneration of whole rows of cells in epiphyseal cartilage, hyperplasia and hypertrophy of cells in different layers of the epiphyseal cartilage, chondrophyte and cartilaginous covering of the joint (Silberberg and Silberberg).

[In the light of these results it is interesting to speculate as to whether the anterior lobe of the pituitary plays any rôle in the production of degenerative changes in human cartilage which antedate primary hypertrophic arthritis.—Ed.]

The Silberbergs also noted the effect of thyroid extract and of potassium iodide on the bone and cartilage of immature guinea-pigs. Thyroid hormone caused slight hyperplasia, marked hypertrophy and an accelerated differentiation of euhyaline cartilage of epiphyseal line, ribs, joints and vertebrae. Potassium iodide had a stimulating effect on the proliferation and differentiation of euhyaline cartilage, but also produced retrogressive processes in cells and intercartilaginous matrix, slight absorption of bone, and destructive changes in joints caused by chondroclastic activity.

The lesions of cartilage and bone resulting from experimental scurvy in guinea-pigs were described (Ham and Elliott).

Physiology of Muscles. Despite the fact that the chronically stiff, aching muscles of hundreds of thousands of Americans daily make their lives uncomfortable and unhappy, we know little or nothing about the altered physiology of diseased muscles even in such common states as muscular rheumatism or "fibrositis." Compared to joint tissues human muscle is much more available for biopsy and study, but most physicians would not know how to examine chemically a piece of diseased or painful muscle after

removal. Data on the physiologic reactions of normal muscle are rather extensive but only a pitiably small amount has been applied to the treatment or understanding of muscle diseases. Would not the coördinated efforts of a rheumatologist, a clinical pathologist and a physiologist or student of muscle chemistry be most fruitful if directed to a clinico-chemical study of diseased muscles? There must be many chemical discoveries of great significance, just waiting for the application to diseased muscles of analytical methods already available and already used on normal muscle. Their application might do much to elucidate the cause, for example, of muscle weakness in atrophic arthritis, of muscle stiffness and pain in fibrositis or muscular rheumatism and of the "eternal tiredness" present in both these diseases. To such a group of investigators a number of current [58, 170, 272, 381, 580, 620, 633, 704, 869, 895, 903] reports should be of interest, especially those on the chemistry of muscle contraction,[823] the effect of exercise on blood, lymph and muscle in relation to muscle soreness,[109] the chemical composition of voluntary muscle in muscle disease (including one case of "diffuse myositis"),[799] observations on referred pain arising from muscle,[526] differences in temperature of skin and muscles of lower extremities following various procedures,[337] and on the estimation of fiber, fat cells and connective tissue in muscle.[45]

"Comparative Rheumatology": Rheumatic Diseases in Animals. Horses suffer rather uncommonly with spondylitis ankylopoietica, but commonly with spondylitis osteo-arthritica "as met with in man," according to Mitchell whose necropsy studies on horses with osteo-arthritis suggested that the disease called "shivering" (tremors in voluntary muscles, difficulty in using hind legs) may be due to the pressure of exostoses on nerve roots going to the lumbosacral plexus where they emerge from the intervertebral foramina. Fusion of osteophytes and ankylosis in the lumbar region frequently occur in hypertrophic spondylitis in animals (in contrast to its rarity in humans so affected). Degeneration of intervertebral disks occurs in old horses.

The Campaign against Rheumatism

During the year under review the progress made in the campaign against rheumatism was considerable even though unspectacular. The world-wide extent of the scourge and its huge cost in terms of economic loss and human suffering were made only too clear at the International Congresses on Rheumatic Diseases held at Oxford and Bath which were attended by about 375 delegates from 23 countries. A summary of what is being done to further the campaign in the various European countries was made by Fox. In some countries medical research on rheumatic diseases has increased greatly. Other countries are devoting themselves mainly to new efforts along the lines of prevention and cure; still others are chiefly occupied in educational work and propaganda to improve the occupational and social conditions of rheumatic persons.

England was accused recently of having "the greatest culture with regard

to the study of rheumatic diseases and the worst organization, for the attainment of practical success." [241] But British physicians are doing their best to refute the charge. Since 1929, when the first step was taken in the establishment of the Red Cross Clinic for Rheumatism in London, much has been done, culminating in the formation (1936) of the Empire Rheumatism Council. This council has the earnest support of the Ministry of Health [365]; already its influence is being felt and its work extended to the dominions and colonies.[267, 314, 728] The objectives of the Empire Rheumatism Council were described again in detail.[467, 1033]

Requisites necessary for the success of any campaign against rheumatism include (1) the establishment of an intelligence department to obtain adequate information on all phases of the problem, (2) a definite policy and plan of action, (3) action (Fox). Since "few campaigns can afford to wait until intelligence is complete" tentative, even experimental, advances are fully justified.

According to Davidson and Duthie the problem of rheumatism has not and will not be solved by the spas and voluntary hospitals as they are now run. Voluntary hospitals do not have sufficient beds or physiotherapeutic facilities for the proper management of the great army of rheumatics. Many physicians in the voluntary (i.e., privately endowed) hospitals have little interest in, indeed some have an active distaste for, cases of rheumatism, a distaste born of their ignorance of the disease and what can be done for it. Few physicians in these hospitals have had the special postgraduate training required for the diagnosis and treatment of the rheumatic diseases. "Rheumatology is the most difficult of the medical specialties because of the complexity of the etiology and the diversity of the forms of treatment required." Spas have distinct advantages but are relatively inaccessible for most patients who will not go to spas in the early stages of their disease. The spa hospitals have insufficient beds. The climate at the spas is often suitable only "in-season." Physicians at spas have great difficulty in obtaining adequate follow-up records on the end results of treatment. For these reasons Davidson joined with other British physicians [157, 207, 212, 329, 365, 787] in recommending the following as important for the complete success of the campaign in their country.

The recommendations are: (1) the establishment of a central bureau for the collection and distribution of statistics; (2) a study of those public health problems related to the development and prevention of the rheumatic diseases (e.g., poor housing, inadequate food and warmth, etc.); (3) the adoption by public health authorities of legal weapons to cope with these predisposing and precipitating factors; (4) prevention of dietary deficiencies among school children, e.g. by increasing their consumption of milk, (5) training of children in proper posture; (6) extension of the dental service of the National Health Insurance Scheme to increase the dental care of juveniles; (7) prevention of undue fatigue among children and workers; (8) social welfare work among industrial workers to minimize mental as well as physical strain; (9) establishment of rheumatism departments (units) for the care of in-patients in every general hospital, and the enlargement of those now in existence; (10) establishment of rheumatism clinics or centers for the care of out-patients in all cities; these

should preferably be part of a general hospital; (11) establishment of consultation centers connected with large hospitals in various cities; (12) development of research units in these various departments and clinics, groups of clinicians coöperating with a pathologist, bacteriologist, biochemist and physiologist to study the cause of the disease and to determine the comparative value of the manifold rheumatism treatments (the problem is that *too many* people seem to be able to "cure" rheumatism); (13) establishment of one or more postgraduate schools of rheumatology; (14) training of more physicians in this specialty, to be put in charge of the various units and centers and to devote their full time to the prevention and treatment of rheumatic diseases; (the specialist in charge should, wherever possible, hold a university position; although a specialist, he should enlist in the patient's behalf the coördinated effort of all branches of medicine); (15) a uniform plan of history taking; (16) a uniform scheme for estimating results of treatment; (17) increased provisions for physical therapy in cities and towns not possessing a spa; (18) a change in the National Health Insurance to allow panel fees and payments for physical therapy as well as for medicines; (19) an adequate scheme for the supervision by physicians, visiting nurses and social workers, of after care and its maintenance for at least 6 to 24 months after a patient is discharged from a hospital, spa or "center"; (20) a study of comparative rheumatology: how articular diseases affect animals.

Since it is financially impossible for voluntary hospitals to provide sufficient accommodations or means to carry out these activities, the problem must be handled by municipal and national authorities.[240, 241, 307, 787] The scheme should be under government supervision and given governmental financial support as necessary. "The acceptance of the control of rheumatism as a public health function is the most important measure in solving the problem."[241] But public health authorities cannot institute such a scheme without the support of public opinion. Hence according to Davidson, the most urgent problem in connection with chronic rheumatic diseases is political, not medical: the education of the people as to the extent of the scourge so that they will provide the necessary facilities for its elimination. Propaganda with "the right tone" is a most valuable and powerful weapon and physicians should use it unashamedly to further this end (Fenton; Horder). The public must be told about the insidious and serious nature of rheumatism, and that each individual can do certain things to prevent or ameliorate it; the public should know where proper facilities for treatment are and be encouraged to use them. But in using such propaganda an inviolable principle must be "truth in advertisements" lest false hopes be raised. To maintain the dignity of the medical profession all sensationalism must be avoided.[299]

Chief sponsors of the campaign in the United States are the American Committee for the Control of Rheumatism and the American Rheumatism Association. The organization and purposes of this association and the extent of the problems it faces were outlined in bulletins [25] sent to lay members and others. These are intended to supplement the articles on rheumatic diseases published for laymen in "Hygeia."[229] Of the international campaign Sir William Willcox recently wrote, "The movement has past the dangers of infancy and now enters on the stage of vigorous youth." It is sincerely hoped that this "vigorous youth" will not, like so many others,

be lost through the war. It is tragic indeed that the fine cöoperation expressed through the activities of the Ligue Internationale Contre le Rhèumatisme must be temporarily suspended, but it is confidently expected that the campaign, though perhaps retarded by the war, will be renewed with increased vigor afterward, so that the hope of its sponsors may be realized; that perhaps within a decade the rheumatic diseases can be largely brought under control.

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Because their contents were not indexed in the Quarterly Cumulative Index Medicus we inadvertently omitted the contents of two new journals devoted to rheumatic diseases: *The Harrogate Spa Medical Journal* (Harrogate) and *Rheumatism* (London). Their contents will be reviewed in the next Review.

The chairman of the editorial committee for this review will welcome the receipt of reprints from authors of current (1939–1940) articles which will greatly facilitate the preparation of subsequent reviews.

CASE REPORTS

DISSECTING ANEURYSM OF THE AORTA WITH A CASE REPORT *

By Reuben Finkelstein, M.D., F.A.C.P., and Mendel Jacobi, M.D., F.A.C.P., *Brooklyn, New York*

It is a strange fact that dissecting aneurysm of the aorta, which presents such dramatic symptoms and about which so much has been written, is so rarely diagnosed during life. About 500 cases have been reported in the literature of which only 12 were diagnosed ante mortem. The condition usually occurs in patients between the ages of 40 and 70 years suffering from hypertension and arteriosclerosis. Syphilis, which is a questionable etiologic factor, appears to be present in only 10 per cent of the cases. The normal aorta can withstand great internal pressures, from 900 to 1500 millimeters of mercury. Nevertheless, instances of rupture following a sudden rise in pressure have been reported in young individuals in whom no disease of the aorta could be demonstrated. Shennan [1] reports three cases in males aged 13, 23, and 32 years respectively in which the lesion was apparently produced by unusual athletic exertion. In a number of cases trauma appeared to be the direct cause of the aneurysm.

According to McGeachy and Paullin [2] sclerosis of the vasa vasorum causes degenerative changes in the media thereby weakening its structure. Tyson [3] stated that obliterative changes in the vasa vasorum from atherosclerosis or other types of low grade inflammation lead to medial degeneration. He concluded that the aneurysm begins by the rupture of one or more of the vasa vasorum into the weakened media, and that a tear in the intima is not essential to the formation of the dissecting aneurysm, but occurs secondary to its development. On the contrary, Shennan believes that " deleterious agencies " acting to produce degeneration of the aorta, would be more likely to affect the innermost layers of the media than the other portions, because of their poorer blood supply. These deleterious agencies may be toxic or metabolic in character or due to any other cause which will lead to atherosclerosis.[4] Peery [5] reports a case of dissecting aneurysm of the aorta which was probably of rheumatic origin in a 22 year old Negress. In our patient no sclerotic changes were noted in the vasa vasorum.

Most observers, however, are of the opinion that, irrespective of the underlying cause, a sudden exertion in a hypertensive individual increases the blood pressure sufficiently to produce a break in the weakened intima and permits the blood to extravasate rapidly into the diseased media. The extravasated blood may stop at any point in the wall of the descending aorta or burrow its way down into the wall of the iliac vessels or travel upwards to the carotids. Another break usually occurs, from a few moments to many days later, this time in the outer

* Received for publication August 5, 1938.

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coat of the vessel, and the patient dies almost immediately from exsanguination. The exsanguinated blood may accumulate within the pericardial, pleural or peritoneal cavities. In about 15 per cent of the cases the second break occurs at another point in the intima, thereby forming a canal within the aortic wall which often becomes lined by endothelial cells, the so-called "double-barrelled aorta," and the patient may live for many years to die of some other disease. Shennan [6] reported one case of dissecting aneurysm of the aorta which healed completely with obliteration of the sac, the patient subsequently dying from a second dissecting aneurysm.

Males are apparently affected twice as frequently as females. According to Shennan this is true up to 70 years of age because during this period males are more subjected to the stress of life. After 70 years of age the condition is found relatively more frequently in females.

The symptoms are most dramatic. During exertion the patient experiences sudden acute pain in the chest which may be agonizing and tearing in character, almost immediately followed by shock. This pain may last from a few minutes to a number of hours. At times the pain radiates to the back or to the anterior chest wall. Occasionally the pain is located in the epigastrium with radiation to the back thus simulating a perforating peptic ulcer. In our patient the chief symptom was pain in the epigastrium which radiated posteriorly, and which simulated the pain of perforating peptic ulcer.

Case Report

The patient, M. J., a white male, 54 years of age, was admitted to the Beth-El Hospital on October 8, 1937 complaining of constant pain in the epigastric region of one week's duration. The pain was severe, unremitting and radiated directly to the back. It was not relieved by alkalies, food or small doses of morphine, and became progressively worse until the day of admission. During this time the patient had experienced constant nausea but had vomited only once on the day of admission immediately following a meal of milk and cream. There was no hematemesis or melena.

Previous History: For eight years the patient had suffered from gastric disturbances for which he had been treated by private physicians and at two different hospitals. Each time the discharge diagnosis was peptic ulcer. Until a week before admission each episode of epigastric pain was relieved by food and soda. Diarrhea, constipation, vomiting, tarry stools and hematemesis were never present.

Physical Examination: The patient appeared to be well nourished. The head and upper chest were somewhat flushed. The temperature was 101° Fahrenheit. The eyes, ears, nose and mouth presented no abnormal findings.

Lungs: There was dullness over both bases, more marked on the left side posteriorly; a few crepitant râles were heard in the left base in the axillary region.

The heart did not appear to be enlarged; the rate was rapid (100 beats per minute); the sounds were of fair quality; no murmurs were heard. The blood pressure was 190 millimeters of mercury systolic and 110 millimeters diastolic.

Abdomen: There was marked tenderness in the mid-epigastrium towards the right of the median line; tenderness was also elicited over the twelfth dorsal vertebra posteriorly; the spleen was not palpable; the liver edge was just below the costal margin; no masses were felt.

Because of the history of previous attacks and the roentgenologic findings at the various hospitals where the patient had been treated, the location and radiation of the pain which until the present attack had been relieved by food and soda, and the marked tenderness in the epigastric region which was elicited at the time of the examination,

the diagnosis of peptic ulcer was apparently confirmed. The acuteness and steady persistence of the pain during the present attack, as well as the failure of food and alkali to afford subjective relief, gave rise to the impression that the ulcer was penetrating posteriorly, probably into the pancreas.

Laboratory Findings: Blood Count: Red blood cells were 5,200,000 per cubic millimeter; white blood cells were 10,000 per cubic millimeter; hemoglobin was 95 per cent. The differential leukocyte count was as follows: 10 staff cells; 64 segmented polymorphonuclear cells; 4 eosinophiles; 2 monocytes and 20 small lymphocytes. The urine showed no abnormal findings. The blood chemistry showed glucose 107 mg. per cent; urea nitrogen 27.5 mg. per cent; creatinine 1.5 mg. per cent. The blood Wassermann reaction was negative.

The gastric analysis showed the presence of free hydrochloric acid 10° in only one of three fractional specimens. The combined acid reached 30°.

Examination of the feces for occult blood was negative.

Course: On October 10 the patient was still complaining of pain in the epigastrium which radiated to the back, although he was receiving Tr. belladonna 10 minims and Tr. opium 5 minims every four hours. The temperature had risen to 103.5° Fahrenheit. Marked tenderness in the epigastrium was still present. On October 11, the pain in the epigastrium with its radiation to the back became so severe and the tenderness so marked that a perforation of the ulcer posteriorly was feared and a surgical opinion was requested. The patient was too ill to undergo a roentgenologic investigation to confirm the diagnosis of peptic ulcer.

The surgical opinion was as follows: "The patient had suffered from several episodes of epigastric pain lasting for several months at a time, which were eventually relieved by treatment. Roentgenologic examination at different times both privately and at various hospitals suggested the presence of a duodenal lesion. During the past 10 days the patient had suffered from continuous excruciating pain in the epigastrium which radiated to the back, producing at times difficulty in breathing due to diaphragmatic fixation. No definite mass can be elicited in the abdomen, nor is the epigastric tenderness aggravated by palpation. Advise continued sedation to be followed by a roentgenologic study of the stomach which is to be followed by an operation."

Because of the intensity of the pain morphine sulphate, gr. ¼ by hypodermic injection, was then added to the medication as needed.

On October 14 the patient still complained of the epigastric pain which radiated to the back though much milder in intensity.

The next day the patient was more comfortable, was able to take more nourishment, and had a bowel movement following a soap suds enema.

By October 17 the pain had been so much relieved that the morphine was discontinued and the patient prepared for a roentgenologic study of the stomach and duodenum. This was done on the following day. A thorough study by the roentgenologic department failed to reveal any evidence of gastric or duodenal ulcer.

On October 21 the patient still complained of an uncomfortable feeling in the epigastrium, and it was decided to refluoroscope the patient, which was done the same day. At this time the stomach and duodenum were again found to be normal, showing no evidence of a gastric or duodenal ulcer. However, fluoroscopy of the chest revealed a fusiform pulsating dilatation of the entire descending aorta. A roentgenologic film of the chest confirmed the finding of the fusiform dilatation of the aorta (figure 1). A dissecting aneurysm of the aorta was then suspected.

On October 23 the patient stated that he was somewhat improved but still complained of slight discomfort in the epigastrium and posteriorly between both shoulders. An electrocardiogram was ordered but could not be taken in time.

On the morning of October 25 the patient declared that he felt "fairly well" and was able to eat. At 7:15 p.m. of the same day while the patient was on the bed pan he suddenly turned white, vomited, gasped for breath, and expired.

From the third day after admission to time of death the temperature fluctuated between 100 and 102° Fahrenheit. Only twice during this time did it fall to 99°.

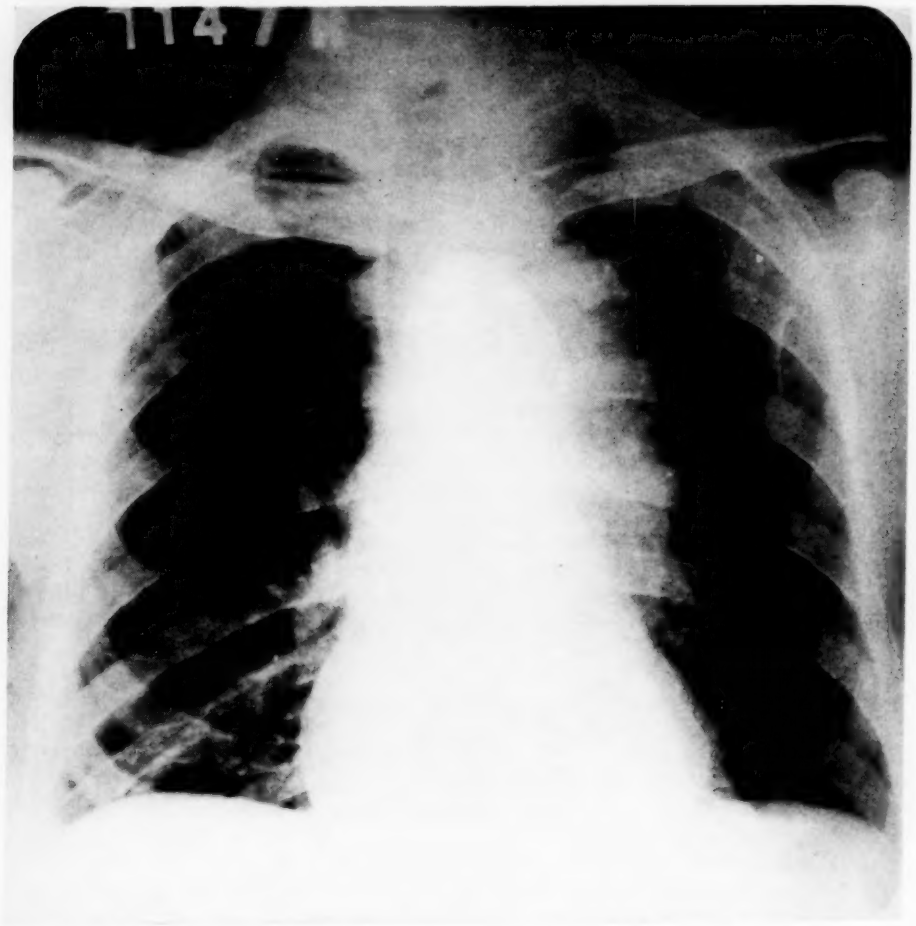

FIG. 1. Six foot roentgenogram of chest showing fusiform dilatation of the descending aorta. The trachea deviated toward the right. No enlargement of the heart.

NECROPSY

Chest: The level of the leaves of the diaphragm was not unduly displaced. The trachea was deviated to the right. The heart was pushed over the left, the apex lying behind the sternum. The left pleural cavity contained about a liter of sanguinous serum and several huge blood clots. The right pleural cavity was free.

Lungs: The pleural surfaces were glistening, showing evidence of anthracosis. The lungs were hypercrepitant throughout and pitted on pressure. The edges could be expressed to paper thinness. At the apices there were several thin walled emphysematous blebs. On section the lungs were dry, the right lung presented a reddish gray appearance, whereas the left lung was of a very pale gray. The trachea and bronchi were clear. The hilar lymph nodes showed no evidence of disease. The pulmonary vessels also showed no changes.

Heart: There was no increase in the pericardial fluid. The pericardium itself was glistening. The right heart was dilated, and the left ventricular musculature was moderately hypertrophied. The myocardium was pale, reddish brown in color and of fairly good texture. The heart chambers were empty. The valves presented no pathologic changes. The coronary arteries showed a moderate degree of intimal lipoid deposition and calcification, without seriously encroaching upon the lumen. The ascending aorta showed little atherosclerotic change but some loss of elasticity. In the arch of the aorta distal to the openings of the left subclavian and left carotid arteries there was a transverse linear break encircling the posterior half of the aorta and extending through the intima into the media. This permitted the escape of blood from within the lumen of the aorta into the wall out beyond the media. The aorta in its thoracic portion presented a blood clot, lamellated and partially organized, about three centimeters thick, lying outside the media and pushing both intima and media into folds into the lumen (figure 2). At the region of the break in the arch blood was present in the loose perivascular tissue resting against the very thin parietal pleura of the apical portion of the left chest. On its pulmonary aspect this pleura was coated with blood and fibrin. Both the thoracic and abdominal portions of the aorta had lost much of their elasticity and contained many lipoid plaques some of which were calcified. An area of atheromatous softening involving both the intima and the media was present near the break in the arch of the aorta. The renal, splenic, and gastric arteries, and some smaller arteries showed a moderate degree of arteriosclerosis.

Gastrointestinal Tract: The esophagus presented no abnormal changes. The stomach was markedly distended, so that the rugae were almost effaced. The mucosa was congested but presented no evidence of recent or old ulceration either in the stomach or in the duodenum. The intestines were moderately distended. The colon contained bile-stained feces in which barium was recognized. Congenital cysts were found both in the kidney and in the liver within the region of the gall-bladder. Another cyst one centimeter in diameter was found in the spleen. No changes were noted in the portal and hepatic vessels.

Microscopic Examination

Aorta: A section was taken from the margins of the break and hemorrhage. The intima was markedly and irregularly thickened, and was composed of dense hyalinized tissue with lipoid deposits. Its endothelium was broken. A vascularization with some round cell infiltration was noted. The media was thinned in places and contained considerable fibrous tissue which was vascularized. No perivascular cellular infiltration was noted in the adventitia.

Aorta: Section through the aneurysm. There was an organized blood clot within the outer part of the media. The adventitia was thickened and fibrosed and contained considerable granulation tissue with round cell infiltration. The outer portion of the media near the blood clot showed degenerative changes.

Elastica-Van Gieson stains on sections of the aorta showed that the aneurysmal dissection took place in the outer portion of the media; a few elastic fibers were seen along the adventitial border of the mass of blood. Some sections showed a severe degree of atherosclerosis and the irregularly thickened intima with considerable hyalinized fibrous tissue. At this point the media showed fragmentation of the elastica and in places fibrous scarring with total replacement of elastic fibers together with vascularization. In such areas, particularly those taken through the point of rupture, there was considerable necrosis of the intima, with necrotic lipoid containing cells admixed with necrotic tissue. In the underlying adventitia there was a rather marked leukocytic infiltration which was also noted near the necrotic intima. None

of the vasa vasorum examined showed endarteritic changes; and whereas in some places perivasavasoral lymphocytic infiltration was present, this appeared to be only part of a general cellular infiltration, which included numerous polymorphonuclear cells. There was no associated intimal cellular hyperplasia of the affected vessels.

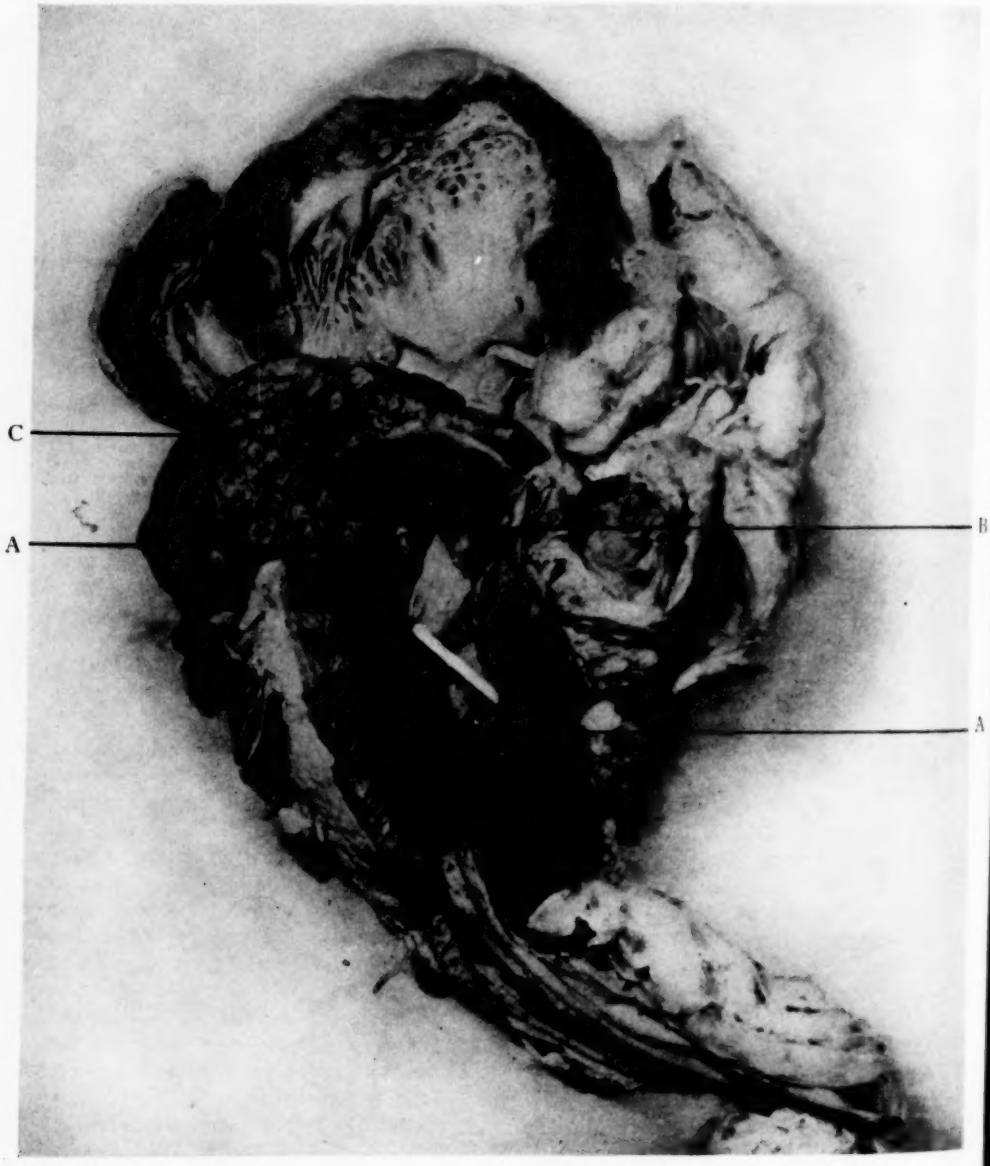

FIG. 2. Heart and aorta. Note the blood clot dissecting in the outer wall of the aorta (*A*). The clot communicates with the aortic lumen through an opening at *B*. At *C* is the extra-aortic blood clot in the left pleural cavity.

Comment

With the large number of patients suffering from hypertension and arteriosclerosis it is most probable that the incidence of dissecting aneurysm of the aorta is greater than one is led to believe by the number of cases reported. Most of these patients presumably die of cardiac failure or coronary artery disease and do not come to autopsy. The true diagnosis will be arrived at only if the symptoms are carefully analyzed and dissecting aneurysm of the aorta is kept in mind.

The sudden onset of agonizing pain in the chest which often radiates to the back in a patient suffering from hypertension, without evidence of acute cardiac or pulmonary disease, should suggest the diagnosis of dissecting aneurysm of the aorta. If the patient lives long enough a roentgenogram of the chest will reveal a fusiform widening of the aorta which on fluoroscopy may or may not be seen to pulsate.

In a number of cases reported by Shennan, Peery and others, and in our case, the outstanding symptom was severe pain in the epigastrium simulating ulcer pain. Indeed a few such patients have been operated upon for peptic ulcer which was not found.

A number of significant findings in our case are of interest. Microscopically the site of primary rupture showed evidence of regeneration and vascularization which bears out the clinical evidence that some time elapsed between the primary intimal rupture and the secondary external rupture. According to the history the interval was at least 25 days, which is much longer than in the average case.

The vasa vasorum were not involved. This would tend to prove that the media, especially the inner layers, may be affected by degeneration due to arteriosclerotic changes in the intima and not necessarily by previous disease of the vasa vasorum as was suggested by Tyson.[3]

Of great clinical interest, however, is the fact that for eight years prior to his last illness the patient suffered from gastric symptoms which led to the diagnosis of peptic ulcer for which he was treated. However, the roentgenologic examination during his last illness and the necropsy findings failed to reveal any evidence of a recent or healed gastric or duodenal ulcer. The dissecting aneurysm of the aorta could be ruled out as a cause of the long standing gastric symptoms because of its recent onset, no more than seven days before the patient was admitted to the hospital. The absence of any pathologic lesions in the liver, gall-bladder, intestines and appendix, eliminates these organs as a cause for the ulcer symptoms.

However, sclerotic changes were noted in the gastric, splenic, and renal arteries. It has been known for a long time that sclerotic changes in the celiac axis or its branches may give rise to gastric symptoms, even to hemorrhage. It is possible that the peptic ulcer symptoms from which our patient suffered for eight years prior to his last illness must have been caused by the arteriosclerotic changes in the branches of the celiac axis.

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TRAUMATIC CHYLOTHORAX: CASE REPORT *

By JOSEPH GORDON, M.D., *Ray Brook, New York*

TRAUMATIC chylothorax is sufficiently uncommon to warrant an additional case report in the literature. The case here reported is the first instance of this condition observed in a series of 3,000 admissions to the tuberculosis division of this institution during a period of 10 years. One might justifiably expect that such cases, if they did occur at all frequently, would often find their way into an institution where diseases of the chest make up a major portion of the admissions.

CASE REPORT

N. O., a white male, aged 31 years, was admitted on August 11, 1937 on the advice of his family physician. The patient had been treated for an upper respiratory infection. In the course of somewhat irregular treatment over six months, fluid was noted in the right chest and on thoracentesis it was seen as a thick creamy fluid. Accordingly, hospitalization was advised by the family physician for treatment of a pleural effusion. The patient was a native of Holland and had worked as an electrician. The past history was non-contributory, since except for the usual childhood diseases, he had always been in good health. The family history was irrelevant. There was no family or contact history of tuberculosis or familial disease. The present illness began about seven months prior to admission with a "cold in the chest" which persisted. He then developed pain over the sternum which continued for several weeks. Only slight improvement was experienced after a course of "injections" for the cold. Some weeks later he again consulted his family physician because the patient noted that he was having fever and was losing weight. Fluid was found in the chest at this time. The patient was confined to bed for three weeks before admission to the hospital.

Physical examination revealed a fairly well nourished and developed white male. He did not appear acutely ill. Some pallor was observed. The examination was negative save for the chest findings. Expansion was limited on the right and resonance was impaired over the lower half of the chest. Breath sounds were diminished to absent in this area and there was decreased tactile and vocal fremitus. A few moist râles were heard posteriorly. The left lung was clear. Examination of the abdomen was negative for masses or tenderness.

Laboratory Data: Urine: essentially negative. Blood: red blood cells 5,390,000, hemoglobin 105 per cent, white blood cells 8,500, polymorphonuclears 56 per cent, lymphocytes 42 per cent, eosinophiles 2 per cent. Wassermann and Kahn tests negative. Blood cholesterol 145 mg. per cent. *Tuberculin test:* two plus. *Sedimentation rate* (Cutler method): 2 mm. in one hour. Repeated sputa examinations including smears, concentrates, cultures, guinea pig inoculations; and likewise gastric aspirate

* Received for publication December 8, 1938.
From the Tuberculosis Service of the Bergen County Hospital, Ridgewood, New Jersey.

examinations were negative for the tubercle bacillus. Chest fluid: thick, creamy, yellow in color, specific gravity, 1.025, cells predominantly lymphocytes; no organisms.

Roentgen-ray: 1. *Chest:* A homogeneous density was present obliterating the right leaf of the diaphragm and extending up to the level of the third rib. Pulmonic markings were clean cut above on the right and throughout the left lung.

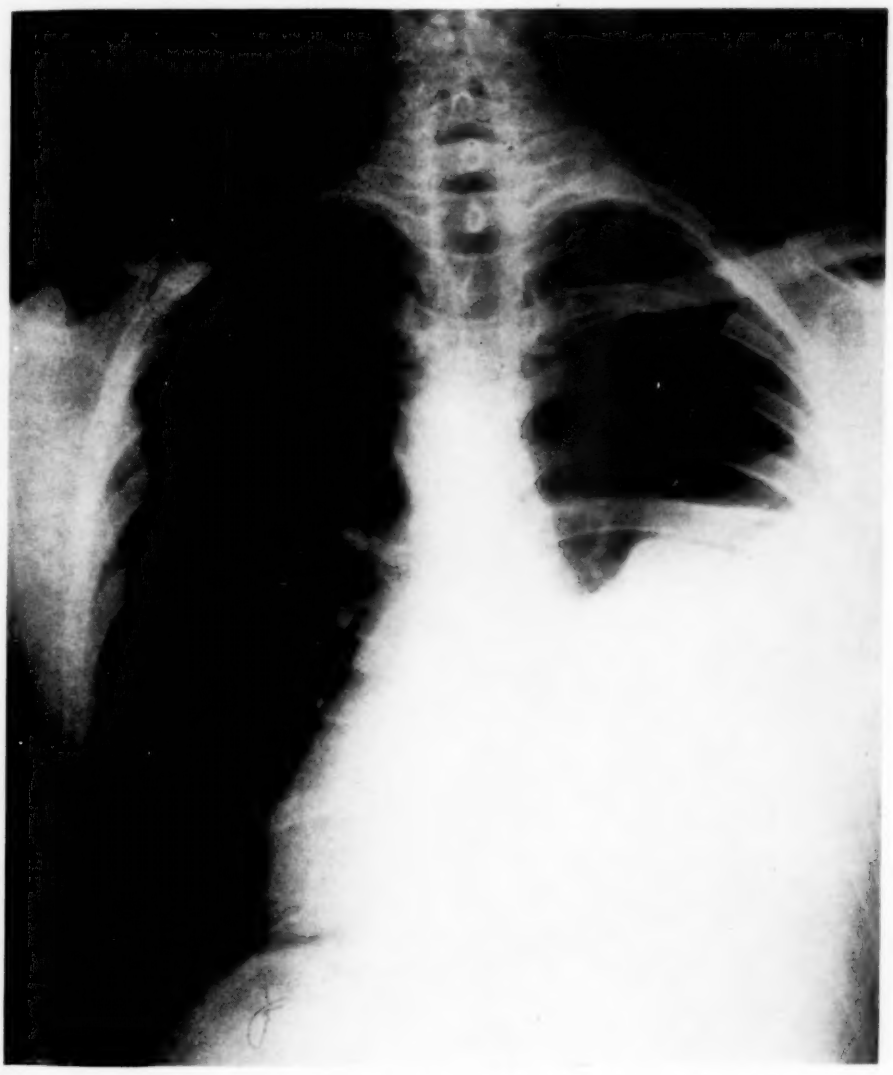

FIG. 1. Admission roentgen-ray showing chylous effusion on the right side.

2. *Abdomen:* Kidney shadows about normal in size. Their lower borders were normal in size and position; the upper border of the right kidney merged with the density in the right thorax.

A tentative diagnosis of pleural effusion was made. The etiological factor on the basis of the history of cough, cold, fever, night sweats with loss of weight, was

considered as tuberculosis. With the absence of organisms and rapid recurrence of this milky fluid, chylothorax was suspected. Fluid in amounts ranging from 950 c.c. to 1500 c.c. was removed on frequent occasions. Its character was unchanged at all times. The fluid was stained with sudan III and fat globules were found on micro-

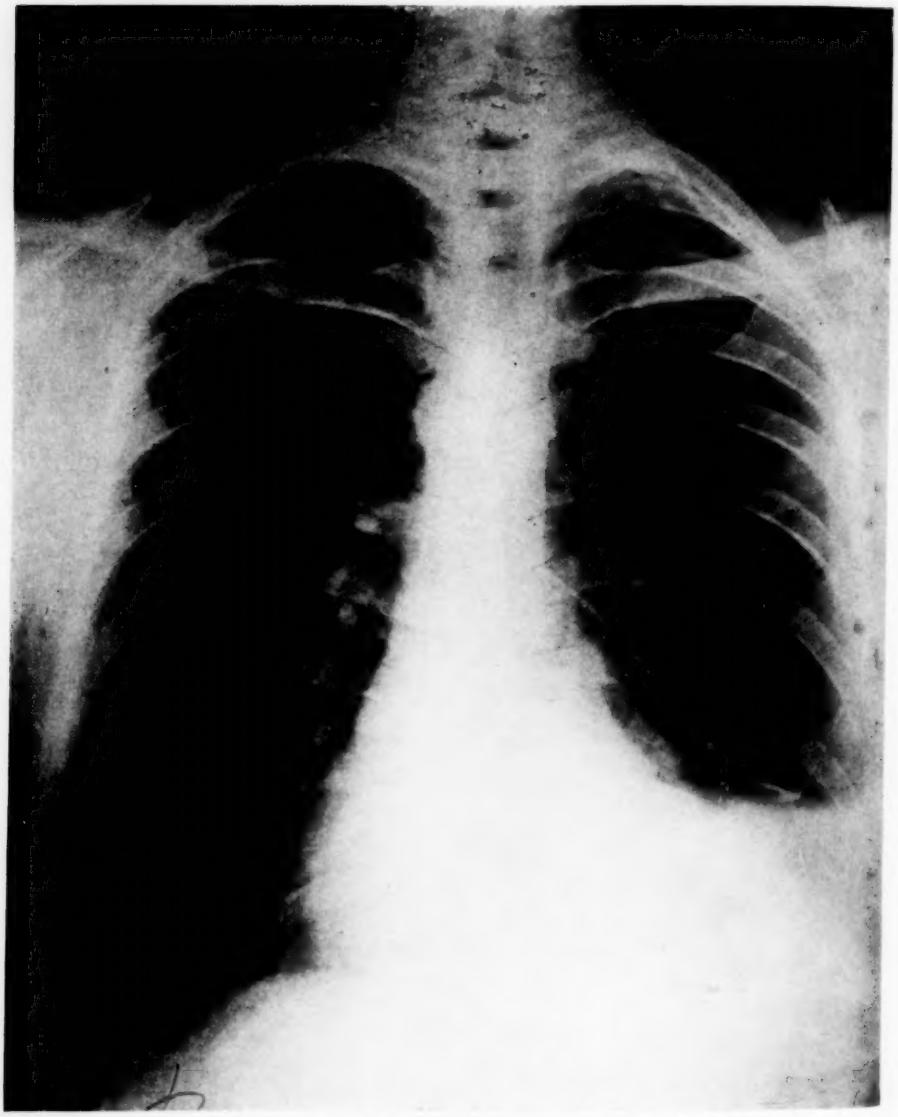

FIG. 2. Roentgen-ray following almost complete evacuation of fluid from chest showing normal lung fields.

scopic examination. On August 13, 1937 the fat content, by the method of Babcock, was reported as 1 per cent. Repeated examinations of the fluid for organisms, both pyogenic and acid-fast, were negative on smears, cultures, guinea pig and rabbit inoculations. Examination of the fluid for possible tumor cells was negative. Further

analyses for fat content showed 3 per cent on two occasions. Following a high fat diet for one week the fluid was reported as containing 4.8 per cent fat. This was then followed by one week on a fat-free diet. The analysis again showed 3 per cent.

Course of Treatment in Hospital: The patient was put on absolute bed rest and received symptomatic treatment including diet and chest aspirations when indicated. Bi-weekly aspirations were done for three months when the fluid began to show a decreased tendency to formation. The chest was irrigated with a 1:3300 saline solution of azochloramid. This was followed by a slight febrile reaction which lasted for five days, ranging between 101–103° F. The patient gradually improved and was allowed out of bed. From an admission weight of 157 pounds his weight increased to a present weight of 174 pounds. Although the fluid is extremely slow in reforming, requiring aspiration once a month, the patient is still being kept under observation.

When the diagnosis of chylothorax was made, it was necessary to determine the etiological factor. No history of an illness of any sort could be obtained. The several factors which might give rise to chylothorax as outlined by McNab [1] (table below) were carefully considered.

CAUSE OF CHYLOTHORAX

Table from McNab [1]

I. Trauma
  1. Closed trauma
    (*a*) Without fracture of bones
    (*b*) Accompanied by fractured ribs, clavicle or vertebrae
  2. Operative wounds
    (*a*) Duct severed
    (*b*) One or more terminals severed
  3. Gunshot or stab wounds
II. New growths and granulomata outside duct: carcinoma, lymphosarcoma, tuberculous glands.
III. Thrombosis of left subclavian vein
IV. New growth within duct
V. Perforating lymphangitis
VI. Aneurysm of duct
VII. Cirrhosis of liver
VIII. Filaria

After reviewing with the patient his past history, it was found that about a month prior to the onset of his present illness he received a rather severe blow on the chest accidentally during his work. Although the blow was rather forceful and caused some momentary discomfort he continued with his work. In the absence of any other explanatory factor, it was hypothesized that an injury to the thoracic duct was sustained at that time. This was perhaps precipitously manifested when the upper respiratory infection, associated with severe coughing, completed the rupture of the duct. Obviously, this theory is grossly lacking in proof, nor can proof of the etiology be obtained from a patient who is recovering from his injury. In the absence of evidence of another cause it was felt that trauma was the most likely etiologic factor in the thoracic duct injury.

In 1931 Van Nuys [2] was able to collect 66 cases of chylothorax of all types. Apparently involvement of the peritoneum is somewhat more common than the pleura, occurring about twice as often.

Shackelford and Fisher [3] recently carefully reviewed 41 cases of traumatic chylothorax from the literature while reporting 2 of their own. Injuries to the chest giving rise to chylothorax were numerically tabulated as follows:

CAUSES OF TRAUMATIC CHYLOTHORAX

Crushing injuries	17
Wounds (bullet and stab)	8
Fall from height	6
Blow on chest	5
Thrown against front seat of auto	4
Hyperextension	1
	41

Crushing injuries were the most predominant causative agents. Great violence is by no means essential, however, nor is it necessary to sustain injury to the bony skeleton.

The manner whereby the thoracic duct is injured is not always clearly ascertained. Where nearby structures such as the clavicle, ribs or vertebrae are injured, the close proximity of the duct explains the likelihood of its being torn or even perforated by a bony fragment. The manner of injury is also obvious in cases of gunshot or stab wound. One of the earlier case reports was made by Finkelstein [4] in 1901. Here too was mentioned incidental injury to the thoracic duct in surgical operations in the neck region, as in the removal of a cervical tumor. Sudden changes in hydrostatic pressure have been offered as a possible explanation of rupture of the thoracic duct in other instances.

The possibility of injury to the duct to a lesser degree than would cause its rupture seems reasonable. A secondary factor of severe cough occurring sometime later might completely rupture the duct by a sudden change in hydrostatic pressure. This theoretical explanation suggested itself in the above case. Although there is a latent period of one month, an even longer period was noted in the case report of Beatty.[5] In this case an automobile accident occurred in June 1928 and symptoms developed in January 1935 following a "cold." Here too the latent period between traumatic injury and the appearance of definite symptoms is only conjecture.

In the entire series of 41 collected cases of traumatic chylothorax, the distribution as to the side of the chest in which the fluid was found, is shown in the following table (Shackelford and Fisher):

LOCATION OF EFFUSION

	Open Injuries	Closed Injuries	Total
Left chylothorax	9	5	14
Right chylothorax	2	18	20
Right chylothorax with chylous ascites	0	1	1
Bilateral chylothorax	1	4	5
Bilateral chylothorax with chylous ascites	0	1	1
Left chylothorax with chylous ascites	0	0	0
	12	29	41

The appearance of the chylous fluid on one or the other side of the thorax seems to bear some relation to the location of the perforation in the anatomical course of the duct. It enters the thorax through the aortic hiatus, somewhat on the right side and gradually inclines to the left, crossing at about the level of the fifth dorsal vertebra. Here it reaches the superior mediastinal cavity when the ascent continues on the left into the neck. The duct empties into the venous system at the angle of junction of the left subclavian vein with the left internal

jugular vein. Occasionally it may divide into two branches in the thorax. It would therefore seem that injuries which occur low down in the course of the thoracic duct would account for the effusion presenting itself on the right side; those occurring higher up would explain the presence of the chylous fluid on the left side. In several of the autopsied cases the location of the perforation of the duct coincided with the presence of the fluid on the right or left side of the chest. However, in Heppner's [6] case the perforation was seen 2.5 cm. above the diaphragm and chyle appeared not only in the abdominal cavity, but also in both pleural spaces.

The thoracic duct lies extrapleurally with relation to the covering of the lungs. In instances where a perforating injury also includes the parietal pleura, leakage into the pleural cavity is obvious. When the rupture is only of the duct itself, entrance into the pleural cavity probably occurs by leakage through the pleura, or through a perforation of the pleura caused by local pressure necrosis. A satisfactory explanation for bilateral effusion is still lacking except on a similar basis.

The diagnosis is dependent upon thoracentesis and careful examination of the fluid. Lillie and Fox [7] mention the striking clinical features as: (1) the latent period before the onset of the symptoms; (2) the rapid re-accumulation of the fluid within the chest after aspiration; (3) the gradual progressive emaciation which frequently ends in death. According to Wallis and Schölberg [8] the specific gravity of true chylous fluid should be above 1.012. In this case the specific gravity was 1.025. Microscopic examination of the fluid for fat droplets which take the sudan III stain is confirmatory and a quantitative analysis for the percentage of fat present rules out the possibility of pseudo-chylous fluid. In addition, a further confirmatory test was added by noting an increase in the amount of fat in the pleural fluid following the ingestion of a high fat diet.

That chyle is essential for the maintenance of nutrition is reasonably well established. The normal flow of lymph from the thoracic duct is from 130 to 195 c.c. per hour. It might be well to point out at this time that the patient showed a weight loss on a fat-free diet, although calorically the diet was apparently adequate. After returning to a regular diet the weight gain as previously evidenced was rather steady and well maintained.

Of the 41 reported cases, 19 died, indicating that the mortality in traumatic chylothorax is strikingly high. Aside from shock and severe injury in these cases, the fact that treatment is non-specific, varied and generally unsatisfactory may be partly responsible for this.

Treatment may be classified under three general headings: (1) Drainage (either by thoracentesis or rib resection); (2) diet (usually low fat); (3) intravenous or oral administration of chyle. Combinations of 1 with 2 or 3 have also been used in certain cases. Rectal feeding was suggested by Hall and Morgan,[9] the rationale being that the lymphatics in this region would absorb the foodstuff and enter the superficial lymph system, thereby circumventing the thoracic duct. Van Nuys [2] used high voltage roentgen-ray in the region of the lower mediastinum in addition to aspiration. Operative repair or ligation of the duct in such cases is not feasible for two reasons: (1) generally the patient is in poor condition; (2) the site of rupture of the duct is rather inaccessible technically. Repair of the thoracic duct in the neck region, however, has met with success in the instances when it was used.[10, 11]

The highest percentage of reported recoveries occurred in those cases treated by thoracentesis alone. This was the elected method of treatment in the above case. The ultimate outcome cannot be accurately prognosticated, but the present indications are that it will be favorable.

Summary and Conclusions

1. A case of chylothorax of likely traumatic origin is presented.
2. The mechanisms responsible for rupture of the thoracic duct are cited. In the above case there seemed to be a combination of two etiological factors.
3. The diagnosis is entirely dependent upon thoracentesis with examination of the fluid for fat droplets and other studies.
4. The high mortality is mentioned and the methods of treatment enumerated.
5. Repeated thoracentesis evidently yields the best results.
6. An apparent favorable outcome in this case has been obtained by the above-mentioned method.

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EDITORIALS

THE TWENTY-FOURTH ANNUAL SESSION

The Twenty-fourth Annual Session of the American College of Physicians at Cleveland not only drew a very large attendance of physicians but richly repaid them for coming. The program of General Sessions, Morning Lectures and Panel Discussions had a consistently large audience. Indeed the latter were so popular that many who applied late were unable to obtain tickets.

The program provided by the hospitals and medical schools as ably organized by the General Chairman, Dr. Karsner, was enthusiastically praised. In addition to all these intellectual advantages offered by the meeting, the members of the College will remember with pleasure the cordial greetings given to the College by the medical profession of this splendid medical center, Cleveland.

BLOOD FOR BLOOD CULTURES

The striking advances in specific chemotherapy have increased the importance of isolating the etiologic organism in any acute infection. This may be possible at times by surface cultures or by bacteriologic studies of sputum, urine, spinal fluid, or exudates in the pleura, joint cavities, etc. There is, however, in some of these instances, especially in surface throat cultures, sputum cultures and urine cultures, a degree of uncertainty as to whether the organisms obtained are identical with those causing the constitutional symptoms. Since bacteria in the blood stream may be assumed to be etiologic agents, and since their presence there moreover indicates a dangerous invasion of the whole body, the use of the method of blood culture is universal in all cases of sepsis.

It may be questioned, however, whether the routine method of obtaining blood for blood culture from a vein in the arm is always the most delicate method of determining an invasion of the blood stream or of identifying the pathogenic organism for therapeutic purposes. In the case of thrombophlebitic sepsis it has been shown (Friedemann [1]) that blood taken from a vein directly draining the focus of infection contains many more organisms than the venous blood as sampled from another area. This is due in part to the great dispersion of the bacteria in the general blood stream, in part to their destruction, and in part to the filtering effects of the capillary beds through which they may pass. Bacteria from the intestinal tract, for example, must pass the capillary bed of the liver, that of the lung, and that of the forearm or hand before they will reach the veins of the elbow from which blood is taken for culture. Organisms from an infection at the

[1] Friedemann, U.: Bakteriologische Topodiagnostik der Sepsis, München. med. Wchnschr., 1929, lxxvi, 1323–1327.

periphery of the body will have to pass the capillaries of the lungs and of the forearm or hand before they reach the elbow veins. If the infection spreads by lymph channels there will be further filtering out by the lymphoid tissues before the venous system is reached. Bacteria causing lung infections which invade venous channels directly have, however, only the peripheral capillary bed to pass before reaching the arm veins.

It would seem reasonable, therefore, in serious infections at the periphery to utilize whenever feasible a vein draining the infected area as a source of blood for culture. The question of whether in pneumonia arterial blood cultures would possess an advantage over venous cultures sufficient to outweigh the greater technical difficulty and painfulness of the arterial puncture remains unsettled. In a group of cases of septicemia Bock [2] found arterial cultures positive in 15 per cent more of the cases than venous cultures. The method seems worthy of further trial.

[2] Bock, H. E.: Über den Wert der bakteriologischen Sternalmarkuntersuchung, Klin. Wchnschr., Berlin, 1939, xviii, 162–165.

REVIEWS

Lehrbuch Der Augenheilkunde. By Dr. Ernst Fuchs. Enlarged and improved by new work of Dr. Adalbert Fuchs. 917 pages; 25.75 cm. × 18 cm. Franz Deuticke, Vienna. 1939. Marks 27.

It is indeed a pleasure to review a new sixteenth German edition of Dr. Fuchs' well-known textbook on ophthalmology. This work was first published in July, 1889 and has had ten English editions, the last appearing in 1933.

The work consists of 904 pages including the index, with 362 illustrations, a large number of which are colored drawings of pathological lesions, and with 5 colored plates.

The author divides the work into five parts. The first consists of a chapter on physiology of the eye, one upon the general pathology and one upon general therapy. The second part has a chapter on objective examination of the eye and one upon functional testing. The third part takes up the various diseases of the eye with chapters dealing with the conjunctiva, cornea, sclera, uvea (anatomy and physiology), iris and ciliary bodies, choroid, glaucoma, lens, vitreous, retina, optic nerve, lids, lacrymal apparatus, motor anomalies and the orbit. The fourth part deals with refractive errors and their correction, and consists of six chapters, the first dealing with lenses, the second with the optical mechanism of the normal eye, the third with myopia, the fourth with hyperopia, the fifth with astigmatism and the sixth with anomalies of accommodation. The fifth part takes up the operations upon the eye. The first chapter describes the general preparations of both instruments and the patient, the second considers operations upon the bulb, and the third takes up operations upon the adnexae.

It seems that the work has been brought well up to date, and the valuable illustrations of pathological specimens by the younger Fuchs have added materially to its value.

The reviewer wishes to criticize the placing of the colored plates at the end of the book. In his opinion, it would be much more effective to have each one placed in the proper relation to the text.

We hope that this sixteenth edition also, will be translated into English and thereby become available to the large American group of ophthalmologists and internists.

C. A. C.

Classic Descriptions of Disease. Second Edition. By Ralph H. Major, M.D. 716 pages; 25.5 cm. × 17.5 cm. Charles C. Thomas, Springfield. 1939. $5.50.

In these days of practical teaching we are too often apt to forget epoch making observations and classic accounts of disease which can so enliven the background of any clinical subject. Dr. Major has provided an excellent source book of such original contributions to medicine which have served him in his teaching. The work is similar to those recently appearing in the fields of pathology, obstetrics and physiology. The author states that his selection of authors in this collection has been influenced by personal taste and the fact that some diseases have more interesting and extended histories than others. He further states that his selections deal in the main with clinical medicine, and that the fields of bacteriology, therapeutics and neurology have been omitted.

The book is composed of 403 selections from 190 authors arranged in 10 main sections with the following headings: infectious diseases, diseases of metabolism, lead poisoning, diseases of the circulatory system, diseases of the blood, kidney diseases, respiratory diseases, deficiency diseases, allergic diseases, and diseases of the digestive

tract. The author states that in this second edition there are new sections on malaria and yellow fever, and that many of the biographical sketches have been rewritten and the index revised and enlarged.

The material in the book is arranged in the form of succinct biographical sketches of both ancient and modern physicians followed by extracts from the works of these men who have contributed to fundamental knowledge in clinical medicine. These extracts in most instances have been translated (where necessary) and paragraphed by the author with considerable reduction in reading effort as the result. Numerous reproductions of portraits, illustrations and pages from classic works lend color to the book. There is an adequate index and the print is clear. The biographical references are given throughout the book.

Upon finishing the book the reader is determined not to close it permanently but to place it on his reference shelf for frequent use.

J. E. S.

Medicine in the Outpatient Department. An Introductory Handbook. By WINTHROP WETHERBEE, JR., M.D. 111 pages; 15.5 × 12 cm. Paul B. Hoeber, Inc., New York. 1938. Price, $1.00.

If the third year student masters the information and point of view contained in "Medicine in the Outpatient Department," he would indeed be well prepared to take advantage of his dispensary medical course. The author suggests certain simplifications in history taking and physical examination which are necessary because of the usual lack of time for examination and instruction in the outpatient department of a large city hospital.

The reviewer feels, however, that it is unfortunate that students must be introduced to clinical medicine with the aid of shortcuts, but as long as medical instruction in the dispensary is given to third year students this book will fill a definite need. It can be highly recommended and should be widely used.

M. S. S.

Dental Science and Dental Art. Edited by SAMUEL M. GORDON, Ph.D. 731 pages; 24 × 15 cm. Lea and Febiger, Philadelphia. 1938. Price, $9.50.

For the internist interested in focal infection, this book will be a mine of information about his favorite subject. The editor and his collaborators herald the "dentistry of tomorrow based on science." Occasionally repetitious and somewhat grandiloquent in style, the book is full of effective diagrams and tables. The newer work on parathyroids and vitamins is included with laudable conservatism. The section on orthodontia has significance in many allied specialties. Dental caries is discussed from many angles with a thorough display of experimental data and photographs. Vincent's infections are thoroughly analyzed, as are many other medical diseases of the mouth. The art of dentistry does not obtrude itself upon the medical reader.

There are full references at the end of each chapter.

C. A.

COLLEGE NEWS NOTES

Twenty-fourth Annual Session of the College

The Twenty-fourth Annual Session of the American College of Physicians held in Cleveland, April 1–5, inclusive, 1940, proved to be one of the most successful and most largely attended sessions in the history of the College. There were in attendance physicians from 47 States, Hawaii, Puerto Rico, 8 Provinces of Canada and from Mexico. It is interesting to note that physicians came from 476 different communities. The largest number of registrants was from Ohio, with New York second, Pennsylvania third, Michigan fourth and Illinois fifth. A comparison of attendance for the past four years follows:

	Cleveland (1940)	New Orleans (1939)	New York (1938)	St. Louis (1937)
A. C. P. Members	1,221	896	1,447	877
Guest Physicians	710	525	463	589
Medical Students	116	499	3	414
Visiting Women	262	578	319	210
Exhibitors	223	167	291	201
Other Non-Physicians	25	16	24	30
	2,557	2,681	2,547	2,321

The program of General Sessions and Morning Lectures, as well as that of the Clinics and Panels was acclaimed as among the best arranged by the College. It was particularly noted that the Panels proved exceedingly attractive and that many more members sought admission than facilities would permit.

The technical exhibit, limited in size by intent, represented the highest type exhibit of its kind shown at any medical meeting to date. The College Committee on Exhibits and Advertisements has applied a selective system by which undesirable and irrelevant exhibits are eliminated. Each exhibit was selected because it was particularly representative of the interests of Internal Medicine and its allied specialties. High pressure methods and undesirable tactics were debarred. Here was assembled a group of exhibitors of the highest class, manned by gentlemen of training and courtesy. Especially was there an excellent exhibit of medical books, pharmaceuticals, apparatus and appliances.

At the Convocation on Wednesday evening, April 3, President O. H. Perry Pepper delivered the annual presidential address and Dr. Charles F. Martin, Master and ex-President of the College, Emeritus Dean and Emeritus Professor of Medicine of the McGill University Faculty of Medicine, delivered the Convocational address, an interesting and inspiring review of the development of the College.

The transactions of the Board of Regents and of the Board of Governors, together with an account of the Annual Business Meeting of the College, will be published in a later issue of this journal. However, herewith is published the roster of those inducted into Fellowship at the Convocation April 3, 1940, and the list of elections to Associateship on March 31, 1940.

ROSTER OF NEWLY ELECTED FELLOWS, 1939–40

Walter Paul Adams.....Norfolk, Va.
Kenneth Dayton Allison Allen.....Denver, Colo.
John Arthur Alvarez.....Houston, Tex.
Harold Cook Atkinson.....Macon, Ga.
Villairs Thomas Austin.....Urbana, Ill.
Louis John Bailey.....Detroit, Mich.
David W. E. Baird.....Portland, Ore.
Thomas Williams Baker.....Charlotte, N. C.
M. Herbert Barker.....Chicago, Ill.
Douglas Davison Baugh.....Columbus, Miss.
Sim Fields Beam.....St. Louis, Mo.
Marion Foree Beard.....Louisville, Ky.
George Erick Bell.....Wilson, N. C.
Alan Bernstein.....Baltimore, Md.
Walter Reece Berryhill.....Chapel Hill, N. C.
Benjamin Jaffee Birk.....Milwaukee, Wis.
Caryle Bernard Bohner.....Indianapolis, Ind.
James Louden Borland.....Jacksonville, Fla.
Raymond William Brust.....Philadelphia, Pa.
James Arthur Buchanan.....Brooklyn, N. Y.
Burdette Jay Buck.....Hartford, Conn.
Anthony Vandril Cadden.....Hopemont, W. Va.
Coyne Herbert Campbell.....Oklahoma City, Okla.
Edward Guy Campbell.....Memphis, Tenn.
Edward Wyatt Cannady.....East St. Louis, Ill.
Elmer Theodore Ceder.....Baltimore, Md. (U. S. P. H. S.)
Charles Thomson Chamberlain.....Fort Smith, Ark.
Earle MacArthur Chapman.....Boston, Mass.
Clarence Orion Cheney.....White Plains, N. Y.
Benjamin Earl Clarke.....Providence, R. I.
Thomas Alfred Clawson, Jr.....Salt Lake City, Utah
Arthur Ralph Colwell.....Evanston, Ill.
Elias Earle Cooley.....M. C., U. S. Army
Henry Lewis Cooper.....Denver, Colo.
John Cosgrave Corrigan.....Fall River, Mass.
Langdon Teachout Crane.....Detroit, Mich.
Erle Bulla Craven, Jr.....Lexington, N. C.
Lloyd Freeman Craver.....New York, N. Y.
Jacob Antrim Crellin.....Philadelphia, Pa.
James Peter Croce.....New York, N. Y.
Ernest Samuel Cross.....Baltimore, Md.
John Ewart Culp.....Ithaca, N. Y.
Morgan Cutts.....Providence, R. I.
Casimir Joseph Czarnecki.....Toledo, Ohio
James Harold Danglade.....Kansas City, Mo.
Donald Howard Daniels.....Portland, Maine
Harry Anthony Daniels.....Oklahoma City, Okla.
Charles Francis DeGaris.....Oklahoma City, Okla.
Harold Archibald Des Brisay.....Vancouver, B. C., Can.
William Frazier Dobyns.....Aspinwall, Pa.
Stewart Edward Doolittle.....Honolulu, T. H.
George B. Dorff.....Brooklyn, N. Y.

Frederic Griffin Dorwart.....Muskogee, Okla.
Mark Stovall Dougherty, Jr.....Atlanta, Ga.
Charles Hilbert Drenckhahn.....Urbana, Ill.
Charles Dennis Driscoll.....West Collingswood, N. J.
Lucien Young Dyrenforth.....Jacksonville, Fla.
Albert Howell Elliot, Jr.....Santa Barbara, Calif.
Richard Thomas Ellison.....Philadelphia, Pa.
Richard Donald Evans.....Los Angeles, Calif.
Constantine P. Faller.....Harrisburg, Pa.
Harold Fink.....Brooklyn, N. Y.
Philip Finkle.....New York, N. Y.
Trenholm Lawrence Fisher.....Ottawa, Ont., Can.
Greene Smith FitzHugh.....Boston, Mass.
James Murray Flynn.....Rochester, N. Y.
Arthur Conwell Fortney.....Fargo, N. D.
Robert Francis Foster.....Seattle, Wash.
John Henry Foulger.....Wilmington, Del.
Harry Joseph Friedman.....Seattle, Wash.
Mervyn Julius Fuendeling.....Twin Falls, Idaho
Davis Thayer Gallison.....Boston, Mass.
Joseph Nicholas Ganim.....Cincinnati, Ohio
Leon Lloyd Gardner.....M. C., U. S. Army
Henry Napoleon Gemoets.....Houston, Tex.
Nicola Gigante.....Detroit, Mich.
Ralph Lawrence Gilman.....Storrs, Conn.
Kenneth Franklin Glaze.....St. Louis, Mo.
Elmer Edward Glenn.....Springfield, Mo.
Francis Wilcox Gluck.....Baltimore, Md.
Harold Leon Goldburgh.....Philadelphia, Pa.
Jacob S. Golden.....Chicago, Ill.
Grace Arabell Goldsmith.....New Orleans, La.
Richard Emanuel Gordon.....New York, N. Y.
William Hyatt Gordon.....Staten Island, N. Y. (U. S. P. H. S.)
Harold Inman Gosline.....Ossining, N. Y.
Henry Bragg Gotten.....Memphis, Tenn.
Barnett Greenhouse.....New Haven, Conn.
Donald E. Griggs.....Los Angeles, Calif.
Lewis Perkins Gundry.....Baltimore, Md.
Alexander B. Gutman.....New York, N. Y.
Henry Beall Gwynn.....Washington, D. C.
Byron Ellsworth Hall.....Rochester, Minn.
Joseph Franklin Hamilton.....Memphis, Tenn.
Clement Joseph Handron.....Troy, N. Y.
James Fletcher Hanson.....Macon, Ga.
William Pickens Harbin, Jr.....Rome, Ga.
Seale Harris, Jr.....Birmingham, Ala.
Andrew DeJarnette Hart, Jr.....University, Va.
Richard Sylvester Hawkes.....Portland, Maine
Oswald Fenton Hedley.....Philadelphia, Pa. (U. S. P. H. S.)
Morris Abraham Hershenson.....Pittsburgh, Pa.
Edward David Hoedemaker.....Seattle, Wash.
Frank Jackson Holroyd.....Princeton, W. Va.
Ralph Horton.....Oneonta, N. Y.
George Hamilton Houck.....Los Angeles, Calif.

Alson Joye Hull.....Troy, N. Y.
Maurice Spencer Jacobs.....Philadelphia, Pa.
Edwin Bosley Jarrett.....Baltimore, Md.
Sigurd Walter Johnsen.....Passaic, N. J.
George Johnson.....Staten Island, N. Y.
Reginald Franklin Jukes.....Akron, Ohio
Harry Milton Kandel.....Savannah, Ga.
Jerome George Kaufman.....Newark, N. J.
Donald Luther Kegaries.....Rapid City, S. D.
Archibald Donaldson Kennedy.....Louisville, Ky.
Richard Eugene DeMonbrun Kepner.....Honolulu, T. H.
Willard Daniel Kline.....Allentown, Pa.
Albert Preston Knight.....Sayre, Pa.
Edward Kupka.....Olive View, Calif.
Michael Lake.....New York, N. Y.
Wilfred Derwood Langley.....Sayre, Pa.
Sidney Ferring LeBauer.....Greensboro, N. C.
Abbe Alzu Ledbetter.....Houston, Tex.
Thomas Krapfel Lewis.....Camden, N. J.
John Frank Lieberman.....M. C., U. S. Army
Noah Stanley Lincoln.....Mount Morris, N. Y.
John Doyle Littig.....Kalamazoo, Mich.
Arthur Jones Logie.....Jacksonville, Fla.
William Lyon Lowrie, Jr.....Detroit, Mich.
Charles Everard Lyght.....Northfield, Minn.
John Wilfred MacIntosh.....Halifax, N. S., Can.
Lucius Emmett Madden.....Columbia, S. C.
James C. Magee.....M. C., U. S. Army
Norval Mason Marr.....St. Petersburg, Fla.
George Graydon Martin.....Buffalo, N. Y.
John Kay Martin.....Seattle, Wash.
James Carlin McAdams.....Fall River, Mass.
Marsh McCall.....New York, N. Y.
Michael Joseph McInerney.....Washington, D. C.
Emery James McIntire.....Carthage, Mo.
Richard Francis McLaughlin.....Price, Utah
Maud Leonora Menten.....Pittsburgh, Pa.
John Webster Merritt.....Jacksonville, Fla.
Hugh McCauley Miller.....Philadelphia, Pa.
Myron David Miller.....Columbus, Ohio
William Lindsay Miller.....Gadsden, Ala.
John Harold Mills.....Chicago, Ill.
William Rudy Minnich.....Atlanta, Ga.
Robert Thornhill Monroe.....Boston, Mass.
Luis Manuel Morales.....Santurce, P. R.
John Barnhart Morey.....Ada, Okla.
Carl Grismore Morlock.....Rochester, Minn.
Gordon Bennett Myers.....Detroit, Mich.
Walter Cyril Nalty.....San Fernando, Calif.
Franklin Jesse Nelson.....Tulsa, Okla.
Harold Gould Newman.....St. Louis, Mo.
Irwin Louis Vincent Norman.....M. C., U. S. Navy
Robert Bruce Nye.....Philadelphia, Pa.

Harry Clifford Oard.....Jamaica, N. Y.
Richard Ellsworth Olsen.....Pontiac, Mich.
Alexander Pierce Ormond.....Akron, Ohio
Dale Pettigrew Osborn.....Cincinnati, Ohio
Edwin Eugene Osgood.....Portland, Ore.
Samuel S. Paley.....New York, N. Y.
Walter Lincoln Palmer.....Chicago, Ill.
Robert Lawrence Parker.....Rochester, Minn.
Harold Raymond Peters.....Baltimore, Md.
John Peters.....Maywood, Ill.
Manuel de la Pila Iglesias.....Ponce, P. R.
Thomas Antley Pitts.....Columbia, S. C.
John Basil Polansky.....Glenside, Pa.
Herman Marvin Pollard.....Ann Arbor, Mich.
Perry Franklin Prather.....Hagerstown, Md.
Homer Edward Prince.....Houston, Tex.
Meyer S. Rednick.....Ossining, N. Y.
Ivor Ellsworth Reed.....Detroit, Mich.
John A. Reisinger.....Washington, D. C.
Arthur Joseph Revell.....Pittsburg, Kan.
Cornelius Packard Rhoads.....New York, N. Y.
Calvus Elton Richards.....Clifton Springs, N. Y.
Joseph Randall Ridlon.....Detroit, Mich. (U. S. P. H. S.)
Herbert John Rinkel.....Kansas City, Mo.
George Porter Robb.....New York, N. Y.
Milton Edward Rose.....Decatur, Ill.
Joseph Rosenfeld.....Youngstown, Ohio
Thomas Llewellyn Ross, Jr.....Macon, Ga.
Hendrik Marinus Rozendaal.....Schenectady, N. Y.
Julian Meade Ruffin.....Durham, N. C.
Emilie Viett Rundlett.....Jersey City, N. J.
David Robert Sacks.....San Antonio, Tex.
David Salkin.....Hopemont, W. Va.
Russell Lowell Sands.....Santa Monica, Calif.
Irving Henry Schroth.....Cincinnati, Ohio
Albert Andrew Schultz.....Fort Dodge, Iowa
Jacob Schwartz.....Brooklyn, N. Y.
Roy Wesley Scott.....Cleveland, Ohio
Thomas Fort Sellers.....Atlanta, Ga.
Harry Dickey Sewell.....Huron, S. D.
Thomas Palmer Sharkey.....Dayton, Ohio
Jesse Bedford Shelmire.....Dallas, Tex.
Eberle Kost Shelton.....Los Angeles, Calif.
Noble Pierce Sherwood.....Lawrence, Kan.
Elbert Henderson Shuller.....McAlester, Okla.
Harry Willard Shuman.....Rock Island, Ill.
Stanley T. Simmons.....Louisville, Ky.
Frank Anthony Simon.....Louisville, Ky.
Hyman Abraham Slesinger.....Windber, Pa.
Elliott Plummer Smart.....Murphys, Calif.
Leslie McKnight Smith.....El Paso, Tex.
Charles Solomon.....Brooklyn, N. Y.
Reuben Albert Solomon.....Indianapolis, Ind.

James Ward Sours.....Peoria, Ill.
Robert Henry Southcombe.....Spokane, Wash.
Munro Irving Sparks.....Cleveland, Ohio
Tom Douglas Spies.....Cincinnati, Ohio
Charles Henry Sprague.....Boise, Idaho
Thomas Austin Starkey.....Beardstown, Ill.
Henry Barthell Steinbach.....Detroit, Mich.
Gilbert Miller Stevenson.....Gamboa, Canal Zone
James Graves Stewart.....Topeka, Kan.
Merritt Henry Stiles.....Philadelphia, Pa.
Eugene Solomon Talbot.....Chicago, Ill.
David Tenner.....Baltimore, Md.
Chester Quay Thompson.....Omaha, Nebr.
George C. Thosteson.....Detroit, Mich.
John Walter Torbett, Jr.....Marlin, Tex.
James Harvey Townsend.....Boston, Mass.
Frederick Erwin Tracy.....Middletown, Conn.
William Hugh Trimble.....Atlanta, Ga.
Woodford Bates Troutman.....Louisville, Ky.
Pat Alexander Tuckwiller.....Charleston, W. Va.
David Ulmar.....New York, N. Y.
Lee Douglas van Antwerp.....Meriden, Conn.
Stuart L. Vaughan.....Buffalo, N. Y.
Edmond Michael Walsh.....Omaha, Nebr.
Preston Hepburn Watters.....Rochester, N. Y.
Harold Emanuel Waxman.....Pittsburgh, Pa.
Joseph Treloar Wearn.....Cleveland, Ohio
George William Weber.....Albany, N. Y.
Albert Weinstein.....Nashville, Tenn.
Joseph Weinstein.....Brooklyn, N. Y.
Robert Lomax Wells.....Washington, D. C.
George Arthur Westfall.....Halstead, Kan.
Samuel Whitehouse.....Baltimore, Md.
Frederick Rendell Whittlesey.....Morgantown, W. Va.
John Harrington Willard.....Philadelphia, Pa.
Frank Wiley Wilson.....M. C., U. S. Army
George Campbell Wilson.....Wallingford, Conn.
Walter LaFollette Winkenwerder.....Baltimore, Md.
Malcolm Duncan Winter.....Miles City, Mont.
Stanley George Wolfe.....Shreveport, La.
Jonathan Knight Williams Wood.....Troy, Pa.
Burbridge Scott Yancey.....Harrisonburg, Va.
Richard Hale Young.....Evanston, Ill.
Michael Zeller.....Chicago, Ill.
Edwin Eugene Ziegler.....Boston, Mass. (U. S. P. H. S.)
Salvador Zubiran.....Mexico City, D. F.

Elections to Associateship, March 31, 1940

John Delbert Adcock.....Ann Arbor, Mich.
James Moses Alexander.....Charlotte, N. C.
Luis Antonio Amill.....New York, N. Y.
Charles Lee Anderson.....Jackson Heights, N. Y.

James Fleming Anderson.....Los Angeles, Calif.
John Edmund Ashby.....Dallas, Tex.
Richard Bardon.....Duluth, Minn.
George Newton Barry.....Oklahoma City, Okla.
Reuben Berman.....Minneapolis, Minn.
Arthur Bernstein.....Newark, N. J.
Philip George Crosbie Bishop.....New York, N. Y.
Belford Christy Blaine.....Pottsville, Pa.
Leon L. Blum.....Terre Haute, Ind.
Wayne G. Brandstadt.....U. S. Army
Kenneth Arthur Brewer.....U. S. Army
Omar Jesse Brown.....U. S. Navy
Harold J. Brumm.....Rochester, Minn.
Bert Montell Bullington.....Ann Arbor, Mich.
Eugene Paul Campbell.....Philadelphia, Pa.
Lawrence Sherwood Carey.....Philadelphia, Pa.
Harry Dumont Clark.....Denver, Colo.
James Harwood Closson.....Philadelphia, Pa.
Sumner S. Cohen.....Oak Terrace, Minn.
Aloysius John Berchmans Connolly.....Washington, D. C.
Darrell Clayton Crain, Jr.....Washington, D. C.
Joseph David Croft.....Evanston, Ill.
Lester A. Crowell, Jr.....Lincolnton, N. C.
Alexander George Davidson.....Brooklyn, N. Y.
Albert Murray DeArmond.....Indianapolis, Ind.
Paul Mason de la Vergne.....Meriden, Conn.
Karl LaVon Dickens.....New Orleans, La.
Paul Dufault.....Rutland, Mass.
William Miller Dugan.....Indianapolis, Ind.
Herman Franklin Easom.....Sanatorium, N. C.
Hamblen Cowley Eaton.....Harrisburg, Pa.
Francis Busha Edmundson.....Pittsburgh, Pa.
Reginald Campbell Edson.....Hopemont, W. Va.
Eugene Eisner.....Osawatomie, Kan.
Clarence Kilgore Elliott.....Lincoln, Nebr.
Frederick George Elliott.....Edmonton, Alta.
Lowell Ashton Erf.....Berkeley, Calif.
Caryl Ray Ferris.....Kansas City, Mo.
Milton Bayard Filberbaum.....Brooklyn, N. Y.
Meyer Herbert Fineberg.....Cleveland, Ohio
Dan William Fisher.....Lansing, Mich.
Paul Donald Foster.....Los Angeles, Calif.
Leon Jacob Galinsky.....Oakdale, Iowa
Curtis Ferbert Garvin.....Cleveland, Ohio
James Thomas Gilbert, Jr.....Bowling Green, Ky.
Hugh Richmond Gilmore, Jr.....U. S. Army
Herman Coddington Graves.....Grand Junction, Colo.
Frank John Gregg.....Pittsburgh, Pa.
Frank William Halpin.....Fort Worth, Tex.
Charles Edward Hamilton.....Lafayette, La.
Meyer Max Harrison.....Louisville, Ky.
Thomas Haynes Harvill.....Ann Arbor, Mich.
Theodore Henry Harwood.....Burlington, Vt.

Paul Hayes.....U. S. Army
Edward McGowan Hedgpeth.....Chapel Hill, N. C.
Standiford Helm.....Evanston, Ill.
Roger Andrew Hemphill.....Oneonta, N. Y.
Edward Herbert, Jr.....New York, N. Y.
Federico Hernandez-Morales.....San Juan, P. R.
Herman S. Hoffman.....Washington, D. C.
Jesse Morris Horn.....Fort Worth, Tex.
Elbridge Eugene Johnston.....St. Johnsbury, Vt.
John Kenneth Karr.....Milwaukee, Wis.
Thomas Francis Keliher.....Washington, D. C.
William Karl Keller.....Louisville, Ky.
Henry Samuel Kieser.....Reading, Pa.
Jacob Joseph Kirshner.....Philadelphia, Pa.
Morris Kleinbart.....Philadelphia, Pa.
Alva Allen Knight.....Chicago, Ill.
Clarence Lunsford Laws.....Atlanta, Ga.
Edwin Delano Lee.....Exeter, N. H.
Charles Laurn Leedham.....U. S. Army
John Boyer Levan.....Reading, Pa.
Howard Avery Lindberg.....Chicago, Ill.
Eugene John Lippschutz.....Buffalo, N. Y.
Emmett Bryan Litteral.....U. S. Army
Angelo Luigi Luchi.....Wilkes-Barre, Pa.
Frank Luciano.....Richmond Hill, N. Y.
Robert Edward Lyons, Jr.....Bloomington, Ind.
George Carlyle Mackie.....Wake Forest, N. C.
Perry Scott MacNeal.....Ann Arbor, Mich.
William Robert Manlove.....U. S. Navy
Benjamin Markowitz.....Bloomington, Ill.
George Elmer Martin.....Pittsburgh, Pa.
Louis Everett Martin.....Los Angeles, Calif.
Neely Cornelius Mashburn.....U. S. Army
Joseph Ralph Mayer.....Rochester, N. Y.
Merton Melrose Minter.....San Antonio, Tex.
Roger Sherman Mitchell, Jr.....Glens Falls, N. Y.
John Russell Egbert Morgan.....Toronto, Ont.
Mark Tad Morgan.....U. S. Army
Isidor Mufson.....New York, N. Y.
Allison Lee Ormond.....Black Mountain, N. C.
George Colville Owen.....Oshkosh, Wis.
Robert Collier Page.....New York, N. Y.
Victor Louis Pellicano.....Buffalo, N. Y.
Abraham Penner.....New York, N. Y.
Evans William Pernokis.....Chicago, Ill.
Frank Hart Peters.....New York, N. Y.
Kenneth Elwood Quickel.....Harrisburg, Pa.
William Frederick Rexer.....Brooklyn, N. Y.
Ella Roberts.....Philadelphia, Pa.
Albert Henry Robinson.....U. S. Army
William Dodd Robinson.....Ann Arbor, Mich.
Harry Plummer Ross.....Richmond, Ind.
James W. H. Rouse.....San Antonio, Texas

John Griswold Ruth.....Ann Arbor, Mich.
David Ivan Rutledge.....Rochester, Minn.
Milton Samuel Sacks.....Baltimore, Md.
John Philip Sampson.....Santa Monica, Calif.
James Joseph Sapero.....U. S. Navy
Frederick Theodore Schnatz.....Buffalo, N. Y.
Jacob Wolfe Schoolnic.....East Liverpool, Ohio
Henry Alfred Schroeder.....New York, N. Y.
Leon Schwartz.....Philadelphia, Pa.
John Bernard Schwedel.....New York, N. Y.
Edward George Seybold.....Ann Arbor, Mich.
Emory Lee Shiflett.....Louisville, Ky.
William Merrill Silliphant.....U. S. Navy
James Francis Slowey.....Cleveland, Ohio
Frank Edward Smith, Jr.....New York, N. Y.
Leonard Gerard Steuer.....Cleveland, Ohio
Russell Alvin Stevens.....Wilkes-Barre, Pa.
Rendall Risley Strawbridge.....Philadelphia, Pa.
Christopher James Stringer.....Lansing, Mich.
Leonard Neil Swanson.....U. S. Army
Frederick Charles Swartz.....Rochester, Minn.
Verne Wilson Swigert.....Evanston, Ill.
James Sherwood Taylor.....U. S. Army
Rufus Henry Temple.....Kinston, N. C.
Joseph Lawn Thompson, Jr.....Washington, D. C.
William Albert Thornhill, Jr.....Charleston, W. Va.
Richard Nelson Tillman.....Ann Arbor, Mich.
Robert Lane Ware.....U. S. Navy
Hugh Joseph Joachin Welch.....Washington, D. C.
Oliver William Welch.....Fairfield, Ala.
Charles Grant Williamson.....Brooklyn, N. Y.
Olin Glenwood Wilson.....Canton, Ohio
Zolton Tillson Wirtschafter.....Cleveland, Ohio
Raymond Joseph Wyrens.....Omaha, Nebr.

New Life Members of the College

The following Fellows of the American College of Physicians have subscribed to Life Membership, and their initiation fees and Life Membership subscriptions have been added to the permanent Endowment Fund of the College:

Dr. Walter E. Vest, Huntington, W. Va.
Dr. Chester W. Waggoner, Toledo, Ohio

Gifts to the College Library

The following gifts to the College Library of publications by members are gratefully acknowledged:

Books

Dr. Henry Joachim, F.A.C.P., Brooklyn, N. Y., "Practical Bedside Diagnosis and Treatment."
Dr. Luis Manuel Morales, F.A.C.P., Santurce, P. R., "Dirigiendo Al Niño."

Reprints

Dr. Anthony C. Cipollaro, F.A.C.P., New York, N. Y.—2 reprints;
Dr. Lucien Y. Dyrenforth, F.A.C.P., Jacksonville, Fla.—1 reprint;
Dr. Julius Friedenwald, F.A.C.P., Baltimore, Md.—1 reprint;
Dr. Donald W. Ingham (Associate), Washington, D. C.—6 reprints;
Dr. John L. Kantor, F.A.C.P., New York, N. Y.—20 reprints;
Dr. Wilbur F. Keller, F.A.C.P., Oklahoma City, Okla.—2 reprints;
Dr. Manfred Kraemer, F.A.C.P., Newark, N. J.—2 reprints;
Dr. William G. Leaman, Jr., F.A.C.P., Philadelphia, Pa.—3 reprints;
Dr. John H. Musser, F.A.C.P., New Orleans, La.—29 reprints;
Dr. H. M. Read (Associate), York, Pa.—1 reprint;
Dr. Leon Schiff, F.A.C.P., Cincinnati, Ohio—3 reprints;
Dr. Rufus A. Schneiders (Associate), San Diego, Calif.—4 reprints;
Dr. Bernard M. Scholder (Associate), Mt. Vernon, N. Y.—1 reprint;
Dr. James Ralph Scott, F.A.C.P., New York, N. Y.—2 reprints;
Dr. Charles H. Sprague, F.A.C.P., Boise, Idaho—1 reprint;
Dr. James L. Wade (Associate), Parkersburg, W. Va.—4 reprints.

Dr. David Riesman, F.A.C.P., was re-elected president and Dr. Thomas M. McMillan, F.A.C.P., was re-elected vice president of the Philadelphia Heart Association at the 18th annual meeting of this society. Dr. Francis C. Wood, F.A.C.P., was named secretary and elected to the board of directors. Among the others elected to the board of directors were Dr. Mary H. Easby, F.A.C.P., Dr. Louis B. Laplace, F.A.C.P., and Dr. Joseph B. Vander Veer (Associate).

Dr. Ralph H. Boots, F.A.C.P., New York, N. Y., has been appointed Assistant Clinical Professor of Medicine at Columbia University College of Physicians and Surgeons.

Dr. Ross M. Lymburner, F.A.C.P., Hamilton, Ont., was the guest speaker at the meeting of the Sault Ste. Marie Medical Society, at Sault Ste. Marie, Ont., March 9. The subject of the address was "Heart Disease in General Practice."

Dr. Hyman I. Goldstein (Associate), Camden, N. J., has been appointed Editor in charge of the Section on Historical Gastro-enterology of the Review of Gastroenterology.

Dr. R. W. Bradshaw, F.A.C.P., Head of the Oberlin College Student Health Service and Director of Allen Hospital, addressed the American Association of School Administrators at St. Louis, February 25, on "Eye Health of College Students," and spoke on the same subject at a dinner meeting of the Hygiene Club of Kent State University, Kent, Ohio, February 29. Dr. Bradshaw is chairman of the Eye Health Committee of the American Student Health Association and past-president of this organization.

Dr. Herbert T. Kelly, F.A.C.P., Philadelphia, Pa., addressed a meeting of the International Association of Dental Research in Philadelphia, Pa., recently on "A Study of the General Predisposing Factors of Parodontal Disease."

Dr. Barnett Greenhouse, F.A.C.P., New Haven, Conn., was recently appointed Full Attending Physician in Metabolism at the Grace Hospital in New Haven.

The Fifth Annual Postgraduate Institute of the Philadelphia County Medical Society was held in Philadelphia April 15–20, 1940, under the presidency of Dr. Rufus S. Reeves, F.A.C.P. Dr. Edward L. Bortz, F.A.C.P., is President-Elect of the Society.

The program of this meeting emphasized the clinical features of Cardiology, Vascular and Nephritic Diseases. Papers were presented by thirty-two members of the American College of Physicians.

The Northern Medical Association of Philadelphia recently held its 93rd Annual Testimonial Dinner to all living ex-presidents of the Association. Among the members of the College who were honored at this dinner were: Dr. David Riesman, F.A.C.P., Dr. A. C. Morgan, F.A.C.P., Dr. Mitchell Bernstein, F.A.C.P., Dr. Jacob Cahan, F.A.C.P., all of Philadelphia, Pa., and Dr. Hyman I. Goldstein (Associate), Camden, N. J.

Dr. Edward B. Krumbhaar, F.A.C.P., Philadelphia, Pa., was recently elected President of the College of Physicians of Philadelphia.

Dr. Robert S. Berghoff, F.A.C.P., Clinical Professor of Medicine at Loyola University School of Medicine, and Chairman of the Scientific Service Committee of the Illinois State Medical Society, has been elected to membership in the Alpha Omega Alpha Honorary Medical Society in the chapter of his alma mater, St. Louis University. He was inducted at St. Louis on April 24 and on that occasion was the principal speaker. The subject of his address was "Senile Ectasy."

Dr. John H. Musser, F.A.C.P., New Orleans, La., was awarded the Alumni Award of Merit of the University of Pennsylvania School of Medicine on Founder's Day, January 17, in connection with the bicentennial of the university.

Dr. Fred N. Miller (Associate), Eugene, Ore., was elected vice president of the American Student Health Association at its recent annual meeting in New York.

Dr. Nathan Einhorn, F.A.C.P., Philadelphia, Pa., has been named chief and Dr. Leonard G. Rowntree, F.A.C.P., Philadelphia, Pa., has been named consultant of the new department of endocrinology recently opened by the Jewish Hospital.

Dr. Joseph P. Brennan, F.A.C.P., Pendleton, Ore., was recently named president of the Umatilla County Medical Society, which was reorganized during February.

Dr. George Morris Piersol, F.A.C.P., Philadelphia, Pa., was recently named a member of the advisory board of the state department of health by Governor Arthur H. James.

Dr. Elliott P. Joslin, F.A.C.P., Boston, Mass., Dr. James A. Lyon, F.A.C.P., Washington, D. C., and Dr. Allen K. Krause, F.A.C.P., Baltimore, Md., were recently elected to membership in the Medical Council, Veterans' Administration.

Dr. Virgil P. W. Sydenstricker, F.A.C.P., Augusta, Ga., has been awarded a grant of $6,000 by the Markle Foundation to continue his studies on pellagra. Dr. Sydenstricker is a professor of medicine at the University of Georgia School of Medicine.

Dr. Leonard G. Rowntree, F.A.C.P., Philadelphia, Pa., delivered the Roger Morris Memorial Lecture for 1940 at the University of Cincinnati College of Medicine on March 25. The subject of his address was "The Suprarenal Gland and Its Diseases."

Dr. George R. Herrmann, F.A.C.P., Galveston, Texas, was elected secretary of the Texas Club of Internal Medicine at the annual meeting in Dallas in February.

Dr. Thomas N. Spessard (Associate), Norfolk, Va., was elected president of the Neuropsychiatric Society of Virginia at the annual meeting in Richmond, February 7.

Eighth American Scientific Congress

The Eighth American Scientific Congress will be held in Washington, D. C., from May 10 to 18, 1940, under the auspices of the Government of the United States. An invitation on behalf of the President has been extended to the Governments of the American Republics members of the Pan American Union to participate in the forthcoming meeting, which is held in connection with the celebration of the fiftieth anniversary of the founding of the Pan American Union.

The Congress will be divided into eleven sections covering the fields of the various sciences, law and education.

Section V will be devoted to Public Health and Medicine. The program of this section will include sessions devoted to the following topics: education in public health and medicine; nutrition; tuberculosis; chemotherapy; heart disease; cancer; tropical and other diseases of current interest.

There will be arranged a visit to the National Institute of Health with opportunity to observe current investigations in many fields.

The Surgeon General has expressed the hope that there will be a large attendance at the Congress from the members of the American College of Physicians.

OBITUARIES

DR. AUSTEN FOX RIGGS

Dr. Austen Fox Riggs died in Stockbridge, Massachusetts, on March 5, 1940. Dr. Riggs graduated from Harvard with the degree of A.B. in 1898. He obtained his medical degree in 1902 from the College of Physicians and Surgeons of Columbia University and then served for two years as interne in medicine in the Presbyterian Hospital, New York.

In 1904 he became associated with Professor Walter B. James in the practice of general medicine but in 1907 he developed pulmonary tuberculosis. It demonstrates the calibre of the man that he converted this tragic interruption of a brilliant medical career into a stepping stone by which he later achieved eminence in his later chosen specialty of neuropsychiatry.

Advised that a city career was undesirable he retired to the country at Stockbridge and there built up his health and at the same time a private practice in the treatment of functional nervous disorders and also became one of the leading citizens of that charming New England village.

His extraordinary and hitherto unrecognized qualifications for this type of medical practice soon brought to him both success and professional reputation and by 1919 he had gathered support for the fulfillment of his dream to establish an institution which would serve to widen the scope of his activities and particularly to make available to patients of moderate means the advantages of the system of treatment and reëducation which he had developed. So in that year, The Austen Riggs Foundation was established at Stockbridge, with Dr. Riggs as its Founder and Medical Director.

This institution, quite unique in its character, has continued under his direction ever since with increasing prestige and usefulness, not only to the large number of patients who there have sought help, but also to the medical profession. Stockbridge became a center for postgraduate education in this branch of medicine and many are the physicians who during these years have been thoroughly trained there or have been to some degree affected by its influence. This Foundation is a monument not only to Dr. Riggs' rare professional attainments but also to his executive ability and his unusual qualities of leadership.

That Dr. Riggs' capacities could not be confined to a small village and were recognized and deeply appreciated by the outside profession is evidenced by the fact that since 1919 and up to the time of his death he was Consulting Psychiatrist to the Sharan Connecticut Hospital, to the House of Mercy, Pittsfield, Massachusetts, to the Indian Mountain School, Lakeville, Connecticut, to Vassar College where he was also Lecturer and to Williams College.

Since 1922 he has been Clinical Professor of Neurology in the College of Physicians and Surgeons of Columbia University.

In 1937 the honorary degree of Sc.D. was conferred upon him by Williams College.

He was a member of many Boards and Medical Societies, among them The American College of Physicians, The American Board of Psychiatry and Neurology, The American Psychiatric Association, The New York Academy of Medicine, The National Committee of Mental Hygiene and the Massachusetts Society for Mental Hygiene of which he was a member of the Board of Directors.

He was the author of several books and also of numerous articles in medical periodicals dealing with his specialty.

Dr. Riggs has made a great contribution to American medicine. His chosen field is a very difficult one. He cultivated it with a saneness and common sense for which not all workers in this branch of medicine are notable. A thorough student, he was conversant with all the various theories and practices of others, but he possessed the judgment to discard the unsound and to avoid the fads and fancies.

He developed a system quite his own, logical, understandable, and practically successful, which will leave a permanent impress upon the practice of psychiatry, and hundreds of his patients rise and call him blessed for what he has done for them.

Dr. Riggs' record of achievement would have been impossible had it not been for his unusual personality. He was dynamic but sympathetic; forceful but understanding. Appreciative as he was of the innumerable motivations of human behavior he was resourceful in unravelling the tangled skeins and in weaving a new pattern for the conduct of life. He possessed a rare personal charm which added affection to the respect which his patients had for him. This gave him great power which he exercised with restraint and circumspection.

In his family and in his wide circle of devoted friends he was loved to an extent beyond the reach of ordinary men.

He was a rare person. His going has left a gap which cannot be filled.

JAMES ALEXANDER MILLER

DR. JAMES CARPINTER COBEY

Dr. James Carpinter Cobey, aged 65, died suddenly in Los Angeles, California on January 29, 1940 of coronary thrombosis.

He was born in Charles County, Maryland, November 4, 1874. His early education was in the public schools and at Durham Academy. His medical training was obtained at the College of Physicians and Surgeons in Baltimore, Maryland. Following graduation he spent some months on the staff at the Hospital for the Insane at Catsonville, Maryland. He came to Frostburg in the fall of 1896 and devoted his time to the practice of medicine and surgery.

Dr. Cobey was a member and former president of the Alleghany-Garrett County Medical Society. He was also a member of the Medico-Chirurgical Faculty of Maryland and of the American Medical Association and an Associate of the American College of Physicians. He was a member of the staff of the Miners Hospital, Frostburg.

During the World War, Dr. Cobey served in the medical corps first at Fort Oglethorpe and later at the Staten Island Hospital resigning his commission as captain in May of 1919. He remained a member of the Medical Reserve Corps.

His fraternal affiliations included the Elks and the Knights of Pythias. He was a member of the board of Directors of Frostburg National Bank and was a life long member of St. John's Episcopal church and for many years served as a vestryman.

Dr. Cobey and his family were always active and leaders in civic activities and gave large contributions to all charitable organizations and undertakings. He enjoyed a very large practice in this community.

Funeral services were held in Frostburg on February 3, 1940 with burial in the Arlington National Cemetary on February 5, 1940. He will be greatly missed by his patients and his many friends in the profession.

W. O. McLane

DR. WALTER W. BOARDMAN

On February 11, 1940, Dr. Boardman succumbed to a long, chronic illness that had confined him to bed for several weeks before the end came. Walter Whitney Boardman was born December 9, 1883, in Oakland, California. He graduated from the University of California at Berkeley, California, in 1906, entering Cooper Medical College in San Francisco the same year, and obtaining his medical degree at this institution in 1909. Following graduation he served as an interne in the Lane Hospital, part of Cooper Medical School. During the years 1910 to 1912 he was an assistant in Roentgenology and House Officer at the Johns Hopkins Hospital. In 1912 on returning to San Francisco, Dr. Boardman was appointed to the staff of the Stanford University Medical School in charge of the Department of Roentgenology. During the next few years he worked faithfully in this field, but during the World War enlisted in the Navy as a First Lieutenant. On his return to San Francisco at the close of the War he accepted a clinical appointment in Internal Medicine at Stanford University Medical School, becoming interested in the field of gastro-enterology. In 1925 he became an Associate Clinical Professor of Medicine and later was advanced to Clinical Professor. In 1928 Dr. Boardman became a "Fellow" of the College and later became a diplomate of the American Board of Internal Medicine.

He was a member of the San Francisco County Medical Society, the California State Medical Society and the American Medical Association. He had served as Vice-President and President of the California Academy of

Medicine, was a member of the Pacific Coast Interurban Society and the American Gastro-Enterological Association.

His contributions to leading medical journals were numerous and of distinct merit. As an Internist and Consultant, Dr. Boardman stood high in this community, but his ability and zeal were only a portion of his successful attributes, for he had a kindly personality and friendly quality that inspired patients and associates and made lasting friends. His death came at a time when he was at the height of his career and when his help and advice in his County Medical Society were often requested and much prized.

ERNEST H. FALCONER, M.D., F.A.C.P.
Governor for Northern California

DR. JOSHUA M. VAN COTT

Dr. Joshua Marsden Van Cott was born in Brooklyn, N. Y., June 12, 1861, and died February 8, 1940.

Dr. Van Cott received his degree of Doctor of Medicine from the Long Island College Hospital Medical School in 1885. In 1887 he became Pathologist at the Long Island College Hospital and was retained in that capacity until 1924. He also taught Pathology, Bacteriology and Clinical Medicine there until 1917. He had been a Pathology student at the Koch Laboratories in Berlin, Germany, and continued his work in that field through his association with the Long Island College Hospital, where, in 1914, he became Professor Emeritus of Pathology and Clinical Medicine at the Medical School. He was also a Trustee of the Hospital. In connection with his work in Pathology he returned to Berlin in 1891 to obtain for use in this country the tuberculin serum discovered by Dr. Robert Koch.

Dr. Van Cott had been President of the Professional Staff of the Brooklyn Hospital since 1930 and was President of the Board of Trustees of the Hoagland Laboratories attached to the Long Island College Hospital. He became an Attending Physician at the Brooklyn Hospital in 1910, Chief Attending Physician seven years later, and Senior Physician in 1925. He was also a Consulting Physician at the Kings County, St. John's, Wyckoff Heights and the Methodist Hospitals. He was Chairman of Public Health and Education of the New York State Medical Society, 1912–1924 and Vice-President of the same Society, 1927–1928. He had been President of the Kings County Medical Society in 1909, and in 1913 served on the Advisory Committee of the New York Board of Health. He was a founder of the Associated Physicians of Long Island, Member of the New York Academy of Medicine, the New York Pathological Society, the American Medical Association, and had been a Fellow of the American College of Physicians since 1916. He leaves a widow, the former Miss Evelyn Shattuck.

CHARLES F. TENNEY, M.D., F.A.C.P.,
Governor for Eastern New York

ANNALS OF INTERNAL MEDICINE

Official Periodical of the American College of Physicians

Place of Publication—Prince and Lemon Sts., Lancaster, Pa.

Editorial Office—University Hospital, Baltimore, Md.

Executive Office—4200 Pine Street, Philadelphia, Pa.

The Annals of Internal Medicine is published by the American College of Physicians. The contents consist of contributions in the field of internal medicine, editorials, book reviews, and a section devoted to the affairs of the College.

Manuscripts. All correspondence relating to the publication of papers and all books and monographs for review should be addressed to the editor. No manuscripts will be accepted without his consideration. Bibliographic references are to conform to the following style:

4. Doe, J. E.: What I know about it, Jr. Am. Med. Assoc., 1931, xcvi, 2006–2008.

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